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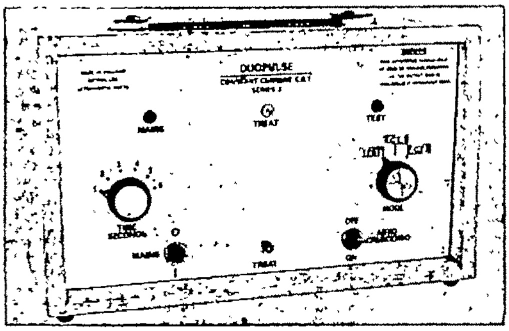

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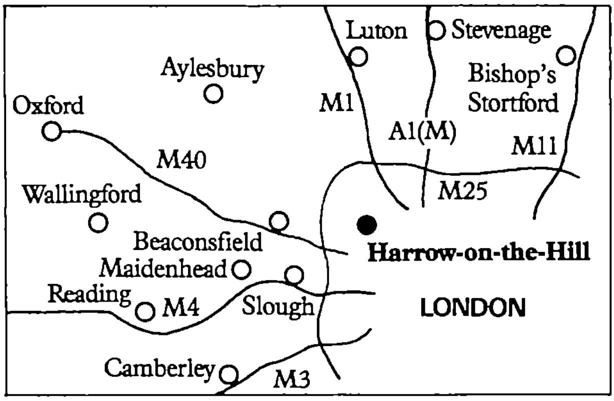

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British Journal of Psychiatry (1986), **148**, 1–11

The Measurement of Social Behaviour in Psychiatric Patients: An Assessment of the Reliability and Validity of the SBS Schedule

TIL WYKES and E. STURT

This paper describes the standard version of the MRC Social Performance Schedule, which covers 21 behaviour areas such as hygiene, initiating conversations, etc. and was designed to be used with long-stay populations, within a hospital or the community. Data on the schedule's consistency over raters, informants, time, and situation showed that the reliability was reasonable over all four areas. The schedule is recommended as a standard instrument to describe the behavioural difficulties of patients likely to be dependent on psychiatric services for some time. Recent data are provided on the levels of problem behaviours found within both long-stay hospitals and community settings, together with references for more detailed behaviour profiles of such groups.

At a time of changing patterns of psychiatric care, it has become important to consider formal techniques that may be used to evaluate the impact of these changes on a patient's status. Research including such assessments has spawned an enormous number of questionnaire, rating scale, and test techniques, of which the overwhelming majority were devised for use with acute patients. But the most exciting of the newer changes in psychiatric care is the transfer of such care from long-stay hospitals to the community. Most recent studies have concentrated on the assessment of social role functioning (Remington & Tyrer, 1979; Platt *et al*, 1980; Tanner *et al*, 1975), but the majority of the long-stay group have long-term disabilities which, although not necessarily intractable, are certainly slow to change. Measures of social functioning are often too gross, and are not designed to detect small changes in behaviour which may allow an evaluation of a service or treatment regime. The detection of small improvements in behaviour also has a secondary function of providing reinforcement for staff working with such patients and motivating them to continue with behavioural or other treatment interventions.

A recent review of assessment procedures used in studies with long-stay patients was highly critical of the number of unstandardised procedures used, the lack of information on their reliability or validity, and an absence of specific descriptions of the patient group under consideration (Hall, 1979). The gap in the assessment literature for the long-stay could be filled by a behavioural measure which has a long history of application in research and which has associated and published psychometric data. This measure is the MRC Social Behaviour Schedule.

Development of the MRC Social Behaviour Schedules

The MRC Social Psychiatry Unit has developed two sorts of performance schedules, both of which have for many years been known jointly as Social Performance Schedules; they came from different roots and measure complementary types of performance. The Social Role Performance Schedule used by Stevens (1973); Vaughn & Leff (1976) and more recently by Hurry *et al* (1983) was based on a schedule published by Stevens & Wing (1976), which was designed to measure how well subjects performed in socially accepted roles such as household management, child care, etc. On the other hand, the Social Behaviour Schedule is a rating scale of specific problem behaviours such as hygiene, initiating conversations, etc., based on work by Wing (1961) and Wing & Brown (1970) with chronic institutionalised populations; it has been further developed in the Unit from work with long-stay populations (Mann & Cree, 1976; Mann & Sproule, 1972; Wykes, 1982) hostel populations (Hewett *et al*, 1975; Ryan & Wing, 1979) and a psychiatric community care population (Wykes *et al*, 1982). The standard version of the Behaviour Schedule is presented here: it was specifically designed to reflect its origins in the assessment of long-term impairment or disability and can be used as an assessment instrument within either a hospital or community care setting.

An overview of the schedule

The schedule covers 21 behaviour areas (see Appendix), which have been shown in previous research to describe the major difficulties exhibited by patients with long-term impairments that usually result in a dependence on or admission to either day or residential psychiatric services. There is some overlap with symptoms that a psychiatrist would expect to treat. Most of the items are rated on a scale of 0 (no problem or acceptable behaviour) to 4 (serious problem), from an informant's description of the patient's or client's behaviour over the past month. The choice of a five-point scale was mainly for historical reasons: during the development of the schedule, this appeared to provide a reasonable description of the range of behaviour problems. The choice of an informant rather than direct observation and the choice of time scale are necessary because some of the difficulties occur infrequently (Nay, 1979). Twenty of the 21 items are highly specific but the final item is 'Other Behaviour', and allows the informant to include idiosyncratic problems that may provoke dependence on psychiatric services or support or are particularly difficult to manage. In previous studies this category has included problems of alcoholism, over- and under-eating, poor memory, etc. but none of these individual problems was common enough to justify its addition as a separate item.

Apart from the profile derived from the individual behaviour descriptions, two further scores can be derived from this schedule; the severe behaviour problems score (BSS) and the mild and severe problems score (BSM). These scores are generated from *a priori* cut-offs on each of the 21 behaviour ratings. Behaviours which have been rated 3 or 4 contribute to BSS and those rated 2, 3 or 4 contribute to BSM.

Assessment of reliability

The consistency of the schedule can be measured over four different factors; rater, informant, time, and situation; the first three of these were investigated in a study of patients at Netherne Hospital, which is reported below. Information pertinent to the situation-specificity of the behaviours rated is given by unpublished data from a study carried out by Wykes *et al* (1982).

Method

Subjects

Sixty-six patients from a variety of placements within the rehabilitation network of Netherne Hospital were selected from a range of day care, stretching from ward care to a rehabilitation workshop where the chances of obtaining open employment were high. Night care arrangements were from a range of 'villas' with different expectations of independence, traditional wards, and patients' own homes in the community. The three major groupings were: (1) attending a community workshop and living in a high-expectation villa or own accommodation; (2) attending a hospital rehabilitation workshop and living in a medium-expectation hospital 'villa'; and (3) attending an OT facility or working on the ward and living in a traditional hospital ward. Basic demographic characteristics are given in Table I. Fifteen to 20 patients were chosen at random from four establishments: a community workshop, a rehabilitation villa, and two long-stay wards, one for men and one for women. The staff interviewed were a workshop supervisor, an occupational therapist, and senior nurses from all four establishments. There were 38 men and 28 women in the study, roughly equally distributed between the types of setting chosen.

The majority of the patients had a long history of psychiatric contact and more than half had a diagnosis of schizophrenia.

(i) *Inter-rater reliability*

The Social Behaviour Schedule as illustrated above requires an interviewer to rate performance given the information provided by an informant. Inter-rater reliability was assessed by two raters attending the same interview: one interviewed the staff member and the other was silent. Twenty eight interviews were rated in this way.

TABLE I
Demographic data

Variable	*Range*	*Median*
Age	21 yrs — 67 yrs	44.5 yrs
Months in night care	1 mth — 44 mths	84.8 mths
Months in day care	2 mths — 44 mths	43.5 mths
Time in in-patient care	0 — 44 mths	48 mths.
Time since first contact with psychiatric services	0 — 49 yrs	16.5 yrs
Age at first contact with psychiatric services	10 yrs — 57 yrs	24.8 yrs
	Primary diagnosis percent diagnosed	*Secondary diagnosis* %
Schizophrenia	52%	17%
Affective disorder	6%	17%
Depression	12%	33%
Personality disorder	14%	0
Other	15%	34%

(ii) *Inter-informant reliability*

Two informants of equivalent staff status, e.g. charge nurse and workshop supervisor, were interviewed about the same patient; to prevent contamination by inter-rater reliability, the same researcher interviewed both members of staff. Forty-four interviews were carried out in this category. Both staff members who acted as informants for a particular patient agreed which of them knew the subject best, and this index informant was used to calculate the test-retest values below.

(iii) *Test-retest reliability*

This form of reliability was assessed by repeating the staff interviews nine months later. As far as possible, the same rater and informant were used for each subject's interview. Fifty-one interviews were carried out.

Results

The social behaviour profile for the sample is given in Table II; it is similar to that found in the series of long-term users of community services (Wykes *et al*, 1982). No one item was shown by more than 40% of the patients. The mean number of problems shown (i.e. with a score of 2 or more for the past month) was 4.3. With the exception of sexual behaviour, each problem was shown by at least 6% of the Netherne patients (see Table II). The overall average was higher than for the Camberwell series (see Discussion and Table V).

Inter-rater reliability

The reliability between raters was high for all but one item of the schedule. Table III gives the percentage agreement and reliability assessment, Kappa (Cohen, 1960) for each of the 21 categories; the calculation of weighted Kappa assumes that the weighting of variables is linear and on a continuous ordinal scale (Cicchetti, 1972). The difference between adjacent codes is equal. The percentage agreement ranged from 84% to 100% with a mean 94%. The Kappa coefficients were all highly significant, except in the category of sexual behaviour problems, where the percentage agreement was high because most people did not score on this item; however, on the four occasions when a problem did occur, there was no agreement as to how it should be rated. There were not enough disagreements on any of the 21 categories for a measure of bias to be calculated.

Inter-informant reliability

Overall, the reliability for items was high (see Table IV); the percentage agreement ranges from 70% to 99% (mean, 86%). All but four Kappa coefficients were highly significant and there were no significant bias effects (see Table III). Only four items appeared to cause particular problems: overactivity and restlessness, acting out bizarre ideas, violence and threatening behaviour and other behaviour. On the first item, overactivity, the disagreements between the informants were major ones—on more than half of the discrepancies, the informants were at least

TABLE II

Percentage of people scoring 2 or more on the Social Behaviour Items

Item	*Wingfield* (*n* = *15*)	*Hedgefield* (*n* = *15*)	*Kemble Morrison* (*n* = *36*)	*Total* (*n* = *66*)
1. Little spontaneous communication	27	20	28	26
2. Incoherence of speech	13	20	11	14
3. Odd or inappropriate conversation	13	20	33	26
4. Inappropriate social mixing	40	40	36	38
5. Hostility	7	27	25	21
6. Demanding attention	7	40	31	27
7. Suicide ideas or behaviour	7	7	11	9
8. Panic attacks and phobias	20	54	25	30
9. Overactivity and restlessness	7	33	8	14
10. Laughing or talking to self	0	7	39	23
11. Acting out bizarre ideas	7	7	7	6
12. Posturing and mannerisms	20	7	26	15
13. Socially unacceptable habits or manners	7	7	22	15
14. Violence or threats	0	7	8	6
15. Depression	7	13	14	12
16. Inappropriate sexual behaviour	0	0	3	2
17. Poor self care	7	20	61	39
18. Slowness	27	20	22	23
19. Underactivity	7	20	19	17
20. Poor attention span	7	7	25	17
21. Other behaviour	33	33	39	36
Median no problems	2.7	3.4	4.9	
People not scoring any problems				

TABLE III
Reliability assessment

	Inter-rater (*n* = *28*)		*Inter-informant* (*n* = *44*)		*Test-retest* (*n* = *51*)		*Inter-setting* (*n* = *26*)	
	Percentage agreement	*Weighted Kappa*	*Percentage agreement*	*Weighted Kappa*	*Percentage agreement*	*Weighted Kappa*	*Percentage agreement*	*Weighted Kappa*
1. Little spontaneous communication	89%	0.525	85%	0.472	82%	0.295	85%	0.337
2. Incoherence of speech	91%	0.581	90%	0.303	88%	0.215	97%	0.581
3. Odd or inappropriate conversation	90%	0.734	86%	0.568	82%	0.472	87%	0.481
4. Inappropriate social mixing	88%	0.684	76%	0.384	82%	0.544	93%	0.720
5. Hostility	94%	0.804	84%	0.262	76%	0.259	88%	0.378
6. Demanding attention	92%	0.810	89%	0.624	80%	0.465	85%	0.411
7. Suicide ideas or behaviour	99%	0.935	94%	0.578	90%	0.210(a)	95%	0.583
8. Panic attacks or phobias	92%	0.744	84%	0.364	73%	0.021(a)	88%	0.310
9. Overactivity and restlessness	96%	0.873	87%	0.170(a)	88%	0.431	83%	0.411
10. Laughing or talking to self	98%	0.944	88%	0.634	86%	0.546	80%	0.361
11. Acting out bizarre ideas	99%	0.843	91%	0.069(a)	92%	0.04(a)	*	*
12. Posturing and mannerisms	95%	0.829	85%	0.611	75%	0.194(a)	91%	0.32
13. Socially unacceptable habits or manners	96%	0.813	88%	0.489	87%	0.404	88%	0.292
14. Violence or threats	100%	1.00	94%	−0.028(a)	94%	0.348	*	*
15. Depression	96%	0.856	86%	0.409	84%	0.227	90%	0.538
16. Inappropriate sexual behaviour	95%	0.176(a)	99%	0.662	96%	−0.041(a)	*	*
17. Poor self care	88%	0.679	87%	0.676	88%	0.709	92%	0.669
18. Slowness	98%	0.898	86%	0.484	84%	0.243	92%	0.415
19. Underactivity	95%	0.744	85%	0.462	79%	0.197(a)	86%	0.235
20. Poor attention span	95%	0.229	80%	0.463	75%	0.346	91%	0.176
21. Other behaviour	84%	0.540	70%	0.177(a)	72%	0.235	71%	0.257

*Not enough variability in ratings to calculate Kappa
(a) weighted Kappa did not reach a significance level of 5%

two divisions apart; in fact, some of the discrepancies were where one informant scored the minimum and one the maximum on the scale. On the item, acting out bizarre ideas (e.g. going to Downing Street because you believe the Prime Minister wishes to talk to you), most of the disagreements were minor, the majority being between an absence of this problem and its presence, but not causing too many difficulties (i.e. between ratings of 0 and 1). It is likely that these disagreements are the result of personal confrontations with the patients' bizarre behaviour, which are not generally reported formally to the staff group. An emphasis on the impairment resulting from such behaviour rather than the description may enable us to get round this particular problem. The third category of disagreements was threatening behaviour and/or violence against property. There were only four occasions when violence was rated, but there was no agreement by the informants on which subjects showed this violence; confusion may have arisen between this item and item 5, hostility—in some cases, hostility may have been rated in preference to violence. In the new edition of the Social Behaviour Schedule, these two items are mutually exclusive. The two new items are (1) violence, hostility, etc. against persons and (2) damage to property.

The final category of disagreement was 'other behaviour'; the overwhelming majority of disagreements were between the presence or absence of a particular behaviour which might impede progress. No changes have been made to the schedule to rectify this difficulty. However, it is recommended that future users should cue informants with several different examples of 'other behaviour' in order to decrease the possibility of missing a behaviour that may be important.

Even though the Kappa statistics were not significant for the four items described above, the percentage agreements for each of these categories was high. When Kappa coefficients were calculated between informants in particular settings, there was still a high level of agreement, which suggests that the categories of informant, e.g. OT, workshop supervisor, and senior nurses, did not affect overall agreement.

Test-retest reliability

Overall, the reliability for items was high: the percentage agreement ranged from 72% to 96% (mean, 83%). Only six Kappa coefficients failed to reach statistical significance (see Table III): suicidal behaviour, panic attacks and phobias, acting out bizarre ideas, posturing and mannerisms, inappropriate sexual behaviour, and underactivity. Most of these items might be expected to change from month to month, but in the category of inappropriate sexual behaviour, most of the disagreements are probably due to rating changes over time (see inter-rater reliability).

When patients were followed-up, a note was made of their intervening psychiatric contact, and this was divided into four categories: no change in overall service level, move to a less supervised setting, a move to a more supervised setting, and a fluctuant course with several moves in and out of various services.

There were no consistent differences in any of these groups, except in the group who moved to a less supervised setting: only one of this group showed no improvement and this person had no problems on either assessment (sign test $P<0.016$).

Inter-setting reliability

Although this study did not test the consistency of behaviour, as measured across settings, data are available which will enable the inter-setting reliability to be assessed. These data were collected from a community sample of patients attending day centres and living in hostel accommodation in the Camberwell area of London (see Wykes *et al*, 1982 for a detailed account of the social performance characteristics of the survey population). The informants in this study were different for each setting, but the raters were the same. The weighted Kappa coefficients are shown in Table III. The percentage agreement ranged from 71% to 97%, with a mean of 88%. Except for the last three items (underactivity, concentration and other behaviours) all the Kappas that could be calculated were significant and in general were higher than the test-retest Kappas. There was not enough variability in the ratings to calculate Kappa for items 11, 14, and 16 because too few people scored at all on these behaviours. No significant bias effects were found.

Categories of behaviours such as underactivity, concentration, and other behaviour may well be exhibited differently in different setting. The day centres provide a structured setting with many constraints on behaviour. However, during the evening, patients have more opportunities and fewer restrictions on their choice of activity. Wykes *et al* (1982) reported more abnormal behaviours in the night settings than during the day, especially under- and over-activity.

Problem behaviour scores: BSM and BSS

As well as using the Social Behaviour Schedule to produce a profile of difficult behaviours, it has also been used to calculate two overall scores, which provide a brief shorthand to the levels of problem behaviours found in a patient or client population. The inter-item correlation (Cronbach's alpha) for the SBS scores (BSM and BSS) lies between 0.71 and 0.75 (see Table IV), which is reasonable evidence in favour of summing across items. Table IV gives the levels of reliability when each of the scores were tested for their consistency over informants, raters, time, and setting. Because the behaviour scores can be measured from 0 to 21, the Kappa coefficient is not appropriate. The reliability assessment was calculated by assuming a model where each of the two sets of data were correlated in a strictly parallel way i.e. assuming the means were equal (SPSS Update, 1981; Kristof, 1963). Probability levels that are found when testing this equal means model against the data should not be significant, since this would lead us to reject the model as an adequate account of the data and to assume that the means were different, and that little reliability exists. Since none of the tests of the model were significant, we can assume that social behaviour scores derived from this schedule are reasonably reliable across raters, informants, settings, and time.

TABLE IV
Reliability of behaviour scores

Type of reliability	*BSM*	*BSS*	*Inter-item correlations*
Inter-rater	0.935	0.938	0.72
Inter-informant	0.911	0.909	0.74
Test-retest	0.665	0.729	0.75
Inter-setting	0.725	0.669	0.71

Discussion

The reliability of the schedule was high across all the parameters considered in this paper—raters, informants, setting, and time; the highest consistency was found between raters. Inter-informant and inter-setting reliability followed, and the least reliable was test-retest reliability (see Table III). The few inconsistencies in the coding of particular items were discussed under the appropriate headings, and some changes to correct for these were suggested. We feel it appropriate to recommend the use of this schedule as a reliable instrument for measuring behaviours in the chronic psychiatrically handicapped. It is relatively easy to administer (given staff goodwill), as only one informant is required and the staff in these facilities are used to making such observations. Some training of interviewers to standardise rating levels is advisable.

It is quite possible to produce a highly reliable instrument for coding behaviour which is not valid, i.e. does not measure what it purports to measure (Lumsden, 1976). However, for the sorts of behaviours that are coded on SBS, direct behavioural observations to check on its validity would be extremely costly. The schedule measures behaviour over the past month, and so an individual would have to be observed over this period for 24 hours per day, as some of the problems occur very infrequently but are still of great concern to those who run community or rehabilitative services. The relationship between SBS as a measure of chronic handicap and other types of measure is described elsewhere (Sturt & Wykes, in preparation).

However, there is some evidence of discriminative validity given in this study and in the study of community services in Camberwell (Wykes *et al*, 1982). A high score (i.e. many problems) is associated with

TABLE V

Levels of problem behaviours associated with different settings

Type of setting		*Mean % of problems (out of 21)*
Netherne series:	Long-stay wards	24%
	Rehabilitation network	16%
Camberwell series:	Day hospitals	10%
	OT/IT centres	19%
	Short stay in-patients (1 yr)	16%
	Supervised hostels	14%
	Unstaffed homes	11%
	"New" long stay group (Wykes, 1982)	54%[1]

[1] Due to the different method of calculation this figure may be slightly overestimated.

a high level of supervision and with a clinical diagnosis of schizophrenia. Table V shows the relative levels of problems in the long-stay wards, the rehabilitation services in the Netherne series, and for comparison, the levels of problems in the Camberwell series.

The schedule is sensitive to changes in status, at least in those people who moved to a less supervised setting; in fact there were few changes in patient status during the follow-up period. The largest group moved to less supervised settings, and these did show few problems at follow-up. It is likely that changes in status over longer periods may provide further clarification of the schedule's usefulness in monitoring changes in behaviour that are predictive of rehabilitative success.

In summary, the SBS schedule conforms to many of the criteria for the usefulness of an assessment schedule (Hall, 1979). Norms are available from different types of service provision, stretching from long-stay hospital to community day and residential services. The sorts of behaviours described are ones that staff feel are important, and no problems that have arisen under the other behaviour category have justified its inclusion as a separate item.

Our findings suggest that it is reasonably consistent between raters, informants, settings, and over time; there is also some evidence of its discriminative validity. The schedule could be used to detect changes in behaviour over time, and therefore provide staff with a more reasonably objective statement of a patient's progress. This sort of feedback is very important in working with patient's whose status changes very slowly.

Finally, there is a great need for a standard behavioural assessment in the area of chronic psychiatric handicaps. This behaviour-orientated approach may prove to be the basis for a culture-free form of assessment, of the kind which cannot be offered by the alternative social role approaches.

Appendix

Social Behaviour Schedule for Administration to Staff Member

Edited by T. Wykes and E. Sturt

In all cases, rate for typical behaviour over the past month—keep reminding informant of this time span.

For items (1) to (25) write a description of the behaviour rated on the coding sheet and code staff attempt to modify behaviour as:—

no attempt to modify behaviour..........................0

attempts to modify...1

Note: The degree (severity) of the behaviour *and* the frequency of occurrence should be taken into account in making the rating. When in doubt, frequency should always carry more weighting than degee.

Write on coding sheet:— setting, date, informant.

Do not write patients' name or address.

Leave staff attempts to modify behaviour till end, and be wary of prompting and cynical about marking down every 'attempt to modify' mentioned. Code only those that seem to be a serious policy of the staff towards the patient.

(1) Communication: taking the initiative

Does S. initiate conversations? Will he or she approach a member of staff either to ask a question or to start a conversation?

If S. approaches will he or she carry on the conversation after the initial comments?

0. Good range of spontaneous contacts. Can initiate a conversation and keep it going by spontaneous contributions. If someone else initiates a conversation, S. reponds appropriately and quite often keeps the conversation going (i.e. active as well as passive response).
1. Can sometimes initiate or maintain a conversation but this is infrequent or the range of topics is very limited. If another person initiates contact S. usually responds appropriately, but only for a short time and then ceases to respond.
2. Occasionally speaks spontaneously, but this is unusual, and limited to greetings, brief factual exchanges etc. Quite often ignores another person's attempt at contact, or turns away.
3. Usually responds negatively to attempts to initiate conversation (e.g. turns away, walks out of the room). Only spontaneous contact initiated by S. himself is non-verbal (e.g. smiling, taking hand, or aggressive contact).
4. S. says virtually nothing. He does not respond when greeted or spoken to. He initiates extremely few verbal or non-verbal contacts.

(2) Conversation: incoherence

How far is S. handicapped in engaging in conversation with others through incoherence of speech?

(N.B. this rating is *not* concerned with how articulate S. is or how intelligently he/she can express himself/herself. The incoherence of speech rated here is that associated with psychotic illness—e.g. flight of ideas, knight's move etc.) (Give example of incoherent speech).

0. No incoherence of speech.
1. Some occasional incoherence of speech (e.g. once or twice a month).
2. Incoherence of speech occurs more frequently (e.g. once a week). Most speech is coherent.
3. Frequent incoherence of speech (e.g. more than once a week).
4. S's conversation is always or almost always characterised by incoherence of speech. Very difficult to understand anything he says.

(3) Conversation: oddity/inappropriateness

How far does S's conversation show a preoccupation with bizarre or eccentric topics, which most people (not only specialists) would regard as extremely odd. Give examples.

0. Above behaviour does not occur.
1. Above behaviour occasionally present (e.g. once or twice a month).
2. Above behaviour occurs more frequently (e.g. once a week) but most speech contains no such examples.
3. Above behaviour occurs very frequently (e.g. daily).
4. Virtually all S's conversation is as described above.

Social mixing: note

The following three ratings are concerned with three different aspects of S's ability to mix with others. These ratings give some picture of the extent to which people have to make allowances for S's handicaps or social difficulties in order to interact with S. Thus S's ratings on these three questions indicate how far he or she is restricted by his or her handicaps to relating only to immediate family or to professional careers.

(4) Social mixing: ability to make social contacts in an appropriate way

If S. was standing at a bus stop and someone asked him or her when the next bus was expected would S. be able to respond appropriately? Would he or she appear odd in manner?

0. S. behaves appropriately in the way he or she makes social contacts with others. Or S. is not interested in making social contacts with others.
1. S. makes social contacts with others appropriately to a degree, but is rather handicapped by lack of grasp of what is and is not socially acceptable (e.g. definitely behaved inappropriately on one or two occasions in the past month).
2. S. can approach others in a socially appropriate manner some of the time but quite often lapses into inappropriate behaviour (e.g. once a week).
3. Most of S's attempts to make contacts with others are inappropriate in nature (e.g. more than once a week but behaviour is not as extreme as (4)).
4. S. is quite unable to behave appropriately and creates frequent embarrassment because of the inappropriateness of his or her attempts to approach others. He/she never or virtually never approaches others in an appropriate fashion.

(5) Social mixing: proportion of social contacts which are hostile in nature

This rating is concerned with the sorts of contacts S. makes with other people. The emphasis in this rating is on verbal or physical hostility. Only rate hostility if it is inappropriate or more extreme than the situation demands. Verbal hostility includes swearing etc. but does not include apathy or failures to respond to a social approach. Only rate physical hostility if S. has had physical contact with another person which was of a hostile nature.

0. Contacts are nearly all appropriately friendly.
1. Mostly friendly contacts. Occasionally contacts are inappropriately hostile (e.g. one or two incidents in past month or more than this but of a relatively minor nature).
2. More frequent incidents of inappropriately hostile contact or a serious incident involving threatening behaviour in past month, but most contacts have been friendly.
3. Most contacts are verbally hostile (e.g. swears, accuses etc. more than once a week).
4. Contacts are frequently verbally hostile, *or* S. has at any time in past month been physically hostile.

(6) Social mixing: attention-seeking behaviour

Does S. try to monopolise peoples' attention? Is he or she resentful if staff members, relatives, etc. give attention to others?

0. S. does not seek attention inappropriately.
1. S. sometimes seeks to monopolise attention but does not get upset if attention is paid to others (e.g. an incident when S. sought to monopolise attention occurred once in past month).
2. S. sometimes seeks to monopolise attention of others, and also tends to get angry and resentful if attention is given to others.
3. S. constantly makes demands on others attention (e.g. more than once a week).
4. S. is constantly making demands on attention of others (either specific others such as a particular relative, or staff in Day Care or Hostel setting, or other people in general). S. also frequently gets angry or resentful if any attention is given to others.

(7) Suicidal and self harming ideas and behaviour

Ratings on this item should be made conservatively. A rating of 3 or more should only be made if the informant was sure that injuries which were sustained were intended by S. to be of a suicidal nature.

0. S. has not spoken of suicide or made any attempt.
1. S. has alluded to suicide indirectly in past month.
2. S. has spoken of suicide directly in past month.
3. S. has made some kind of suicidal gesture in past

month (e.g. scratching wrists). Or S. has spoken of suicide several times in past month.

4. S. has made a serious attempt at suicide or injured himself or herself seriously in past month.

(8) Panic attacks and phobias

This rating is concerned with how far S. is troubled by anxiety, either attached to particular situations (e.g. being with people, travelling, leaving the house) or generalised feelings of anxiety and tension. Preoccupation with health worries is included if there are no objective grounds.

0. S. is free enough from anxiety to be able to undertake any social or other activity he might choose.
1. S. is troubled by occasional anxiety. Or S's anxiety is not excessively disabling because confined to small areas. Or level of anxiety is low enough that S. can contain and live with it.
2. S. is tense and anxious much of the time, and prevents him or her from functioning in certain key areas of life. Nevertheless S. can cope with his anxiety in general.
3. S. suffers anxiety most of the time. Or S. has very frequent (e.g. twice weekly) anxiety attacks. There are few areas where S. can function without being handicapped by anxiety.
4. S. is extremely tense and anxious virtually all the time. His or her anxiety prevents him or her from doing almost anything at all and it troubles him or her constantly.

(9) Overactivity and restlessness

Overactivity should be rated if one or more of the following are present: purposeless pacing up and down or rushing from room to room, frequent unnecessary movements, general restlessness, fidgeting. If either purposeless frequent pacing is present or more than one of the other behaviours is present then rate as marked overactivity.

0. No marked overactivity or restlessness.
1. Occasional periods of restlessness or overactivity (e.g. once or twice in past month).
2. Overactivity occurs quite often (e.g. weekly).
3. S. shows marked overactivity frequently (e.g. daily, or nightly).
4. S. shows marked overactivity for long periods on a regular basis (e.g. most nights spends several hours pacing up and down).

(10) Laughing and talking to self

Only rate here if it is obvious to the informant that S. is not laughing socially i.e. evidence of laughing when alone or muttering so no-one else can catch what is said is enough to consider making a rating.

0. No laughing or talking to self.
1. Occasional episodes of laughing or muttering to self (e.g. once or twice in past month). Can control behaviour if reminded.
2. More frequent episodes of laughing or muttering to self (e.g. three times in past month). S. has some difficulty in controlling behaviour if reminded.
3. Laughing or talking to self occurs often (e.g. weekly).
4. Very frequent laughing or talking to self (e.g. daily). Or less than daily but episodes last a long time.

(11) Acting out of bizarre ideas

This rating is concerned with whether S. decides on some action because of his or her delusions. For example; (a) going to the scene of some major catastrophe because S. feels his or her help is needed. (b) S. assumes that he or she has millions of pounds and so either spends it or tries to spend it on expensive items.

0. No such behaviour.
1. Such behaviour has occurred once in past month.
2. Such behaviour has occurred more than once in past month.

(12) Posturing and mannerisms

(Give examples)

This rating is concerned with odd, stylised movements or uncomfortable or inappropriate postures.

0. No posturing or mannerisms.
1. Some odd or uncomfortable postures or mannerisms occasionally (e.g. once or twice in past month).
2. Behaviour apparent more frequently (e.g. once a week).
3. Behaviour apparent very often (e.g. more than once weekly).
4. Behaviour apparent frequently (e.g. S. adopts odd postures or mannerisms much of the time and every day).

(13) Socially unacceptable habits or manners

This rating concerns unacceptable habits e.g. scratching genitals, passing loud flatus, picking nose etc. Ask particularly about problems at meal times such as poor table manners.

0. Has good manners and behaviour is socially acceptable.
1. Behaviour is not markedly unacceptable but S. has positive qualities in manner.
2. Occasional unacceptable behaviour (e.g. markedly unattractive habit, surliness, uncouthness). However much of the time S. is passively acceptable.
3. Frequent episodes of unacceptable behaviour as in (2) (e.g. once a week).
4. Behaviour is markedly unacceptable most of the time.

(14) Destructive behaviour

Under this item only rate behaviour which results in destruction of property only. If an incident included some threatening behaviour to others as well as destruction of property then rate under item 5 only.

0. S. has reasonable tolerance for provocation, is in control of angry feelings and acts in a socially appropriate manner.
1. Threatens to destroy property occasionally but has not actually done so.
2. Frequently threatens to destroy property.
3. Has damaged property in anger during past month e.g. broken windows, torn clothes.

(15) **Depression**

This rating concerns periods spent in S. sitting with his/her head in his or her hands looking miserable, remarks such as "I wish I had never been born" or "life is pointless" etc. Do not assume suicidal behaviour is an indication of depression other signs need to be present to make a rating here.

0. No such behaviour.
1. Such behaviour occurs occasionally (e.g. one or two brief incidents in past month).
2. Such behaviour occurs fairly often or for fairly long periods (e.g. once a week).
3. Such behaviour occurs frequently (e.g. daily).

(16) **Inappropriate sexual behaviour**

This rating concerns sexual activity which is directed towards another person. *Do not include* self stimulation. Where S. is unaware of social constraints e.g. masturbating in public place but not directed towards any particular person. If unclear whether behaviour constitutes a sexual advance then rate under item 13, socially unacceptable habits. Include discussions of a sexual nature only when they are aimed at provoking the other discussants—if not provoking then rate under odd or inappropriate conversations, item 3.

0. No appropriate sexual behaviour or talk.
1. S. is somewhat preoccupied with sexual matters (e.g. once or twice talked about sex in an inappropriate context in past month).
2. S. more often exhibits inappropriate sexual behaviour (e.g. makes unwelcomed sexual advances).
3. S. exhibits markedly inappropriate sexual behaviour quite frequently (e.g. exposes self, makes unwelcomed sexual advances in an embarrassing manner).
4. S. exhibits behaviour as in (3) frequently (e.g. weekly). S's behaviour is sufficiently marked and frequent to cause problems in his or her household and community.

(17) **Personal appearance and hygiene**

In making this rating, consider cleanliness, hair, changing underwear, incontinence. Also consider bizarre appearance. Take into account the amount of supervision S. receives. If, for example, S. is in a Hostel, consider how S. would care for himself or herself if not in a supervised situation. (Do not consider "fashionable" disorder in dress).

0. Able to look after appearance and cleanliness adequately.
1. Usually appearance is satisfactory but occasionally needs reminding. Or takes an interest in certain aspects of appearance but neglects others.
2. Quite often needs reminding about appearance (e.g. three times in past month). Or attends to appearance but in an inappropriate manner so that appearance is bizarre.
3. Considerable self-neglect most of the time. Needs frequent reminding (e.g. more than once a week) and some supervision.
4. Gross self neglect. No spontaneous care of clothes (e.g. clean underwear) washing hair, hygiene. Needs supervision in all aspects. Would smell if unsupervised. Would be incontinent if not reminded.

(18) **Slowness**

This item is concerned with abnormal slowness e.g. S. sits abnormally still, walks abnormally slowly or is delayed when performing movements. Make allowances for age and physical condition.

0. No abnormal slowness.
1. Moderately slow on occasions, but most of the time is not slow.
2. Moderately slow most of the time, even when stimulated.
3. Moderately slow most of the time with periods of extreme slowness as in (4).
4. Extremely slow. Will sit or lie doing nothing if not stimulated, and even then very slow to move.

(19) **Underactivity**

This rating concerns underactivity only. Bear in mind that S. may be slow (item 18) and underactive or underactive only. Underactivity here is defined as a lack of spontaneous activity. If S. not stimulated will sit and do nothing (moderate underactivity). When it is not possible to stimulate S. into carrying out a task then rate as extreme underactivity.

0. No abnormal underactivity.
1. Moderately underactive on occasions, but most of the time keeps active.
2. Moderately underactive most of the time even when stimulated.
3. Moderately underactive most of the time, with periods of extreme underactivity as in (4).
4. Extremely underactive. Will sit or lie doing nothing if not stimulated, and even then very slow to move.

(20) **Concentration**

Suggested prompts: Does S. find it difficult to concentrate on a task even when he really wants to do so? On watching a T.V. programme? On reading a book? Is S. distractable? Can S. set his mind to something and do it, or does he find it impossible to concentrate long enough to do this?

0. S. does not have problems with his ability to concentrate.
1. S. has periods when he is unable to concentrate.
2. S. can only concentrate for a few minutes at a time.

(21) **Behaviours, not otherwise specified, that impede progress**

Specify any other behaviour or attitude not previously covered, that seems to be holding back S's progress (e.g. smoking, over-eating, anorexia, stealing, obsessions, sleep disturbances). Be conservative in rating. Do not rate behaviours here which should be rated elsewhere.

0. No such behaviour present (other than those rated elsewhere).
1. Behaviours have not occurred in past month but informant worried that they might have done so.

2. Behaviours have occurred a few times during past month.
3. Behaviours have occurred quite frequently.
4. Behaviours have been very frequent.

(22) Type of weekday occupation

0. Unsheltered employment.
1. Sheltered work.
2. Undertakes some work in a day centre, standard of work and punctuality good. Earns pocket money.
3. Undertakes work as in (2) but standard and punctuality poor.
4. O.T.
5. No day time occupation.

(23) Leisure: activities

Rate degree to which S. is able to occupy his or her leisure time, has active leisure interest, and goes out of the house (or hostel etc.) to pursue these.

0. S. has an interest or interests which occupy his or her leisure time and which he or she pursues without encouragement from others.
1. S. shows a bit of active interest in something, but it fluctuates considerably, or his or her interests are bizarre in nature.
2. S. has some rather "passive" leisure interest (e.g. watching T.V.) which occupies him or her to a limited extent.
3. S. might respond fleetingly if somebody worked on engaging his or her interest in some leisure pursuit, but would not keep up interest if left to himself or herself to pursue it on his own initiative.
4. S. has no interest in anything. Even if a relative or professional carer tries to engage his or her interest in some leisure activity, he or she rejects this.

(24) Restrictions on activity

Are any restrictions placed by carers or relatives on the activity of S? (e.g. on money, going out, food, cigarettes etc). Specify on coding sheet.

(25) Unrealistic aims

This item concerns S's expectations about his or her ability to affect changes in his or her own life. It focuses on his or her view of what he or she can realistically aim to achieve in the near future (e.g. the next 3 months). The area in question could include work, housing, personal relationships, ability to overcome impairments, child care etc. (whatever is relevant to the individual).

Suggested prompts: In the past months how realistic would you say S. has been about what he or she can achieve in near future? Does he or she expect too much or too little? About employments? Housing? Overcoming his or her handicaps?

0. The aims of S. are realistic.
1. S. is indifferent to any aims.
2. S. is not realistic in his or her aims and goals. He or she overestimates his or her ability.
3. S. is not realistic in his or her aims and goals. He or she underestimates his or her ability.

(26) Reason for being in setting

(Specify on coding sheet and specify location).

(27) Most difficult problem

Which out of all these problems do you find the most difficult to deal with?
code: 1–25 (number of the item in this schedule)

(28) Physical handicaps

Code 0 — no such handicaps.
1 — physical handicap present (specify).

(29) Other handicaps (not psychiatric)

Does S. have any other handicaps which are not directly associated with psychiatric illness but which impede his progress? (e.g. illiteracy).
Code 0 — no such handicaps.
1 — Handicap present (specify).

(30) Work: quality and attitudes

See coding sheet. Obtain this information from another person, e.g. staff at rehabilitation unit if more appropriate.

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*Til Wykes, BSc, DPhil, *Psychologist, Department of Psychology, Institute of Psychiatry, De Crespigny Park, London SE5 8AF.*

E. Sturt, PhD, *Statistician, Department of Psychiatry, Institute of Psychiatry, De Crespigny Park, London SE5 8AF.*

*Correspondence

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Life Events and Schizophrenia:

A Saudi Arabian Study

M. A. F. AL KHANI, P. E. BEBBINGTON, J. P. WATSON and F. HOUSE

Using an Arabic version of the PSE, supplemented by CATEGO, we selected 48 patients with acute schizophrenia from the population of the Najd region of Saudi Arabia. Their life-event histories for the six months before onset or relapse were compared with those of 62 control subjects. A postive association between events and onset was established only for married women, although there was a parallel trend for men and single women suffering their first schizophrenic episode. The observed impact of life events was limited to the three weeks before onset. These findings are discussed in the light of Saudi culture.

In the last 20 years, psychosocial explanations of the origin of psychiatric disorder have been heavily dependent on life-event research. There is now a clear consensus that *depressive disorders* are generally preceded by a significant increase in the number of life events (e.g. Lloyd, 1980; Paykel, 1982), although many of the details of this relationship have yet to be clarified. Life-event studies have also been undertaken in the investigation of a wide variety of other conditions, both psychiatric and physical, and the many methodological advances of recent years have permitted increasingly firm conclusions to be reached (Bebbington, 1985). Attempts to produce an overall explanation of the development of *schizophrenia* in terms of early influences have not been successful (Hirsch & Leff, 1975), and relatively limited explanations of causation by more immediate stressful situations seem more likely to bear fruit.

'Extreme situations', such as war-time combat or overwhelming natural stresses, do sometimes produce reactions with symptoms of a psychotic type. These are typically described as 'transient' and 'self-limiting', as they disappear rapidly once the individual has been removed from the situation: the evidence that extreme situations can provoke serious and long-lasting clinical symptoms or disabilities in otherwise normal individuals is inconclusive and contradictory (Day, 1981).

The major controlled and systematic studies of life events and schizophrenia are those of Brown & Birley (1968) in Camberwell, London and of Jacobs & Myers (1976) in New Haven, Connecticut. The Camberwell study (Brown & Birley, 1968; Birley & Brown, 1970) investigated 50 schizophrenic patients who had been admitted consecutively to a hospital in south-east London. Onset or relapse in each case was dated to within a week, and had occurred within the three months prior to admission. The diagnostic criteria were essentially Kraepelinian and the PSE (Wing *et al*, 1974) was used in selecting the patients. These patients were compared with a control group which was roughly comparable in age, sex, nationality and education, but differed in marital status, family composition, and degree of contact with close relatives living outside the household. Patients and controls were given the same detailed life-event check-list and the time and context of any reported life event was established. A history was obtained of events during the three months before the onset of florid symptoms (for the schizophrenics) or the three months before the interview (for the controls).

It was found that there was a significantly greater rate of events in the three weeks before the onset of schizophrenia than in the comparable period for the controls: 60% of the schizophrenic group experienced an 'independent' or 'possibly independent' event in this period, as opposed to 19% of the controls (for *our* definition of dependence see below). This compared with rates of around 20% in the schizophrenic group for each of the three 3-week periods making up the remainder of the three months before onset. In a further analysis, Birley & Brown (1970) reported that this finding was independent of type of onset, variations in symptomatology and diagnosis, the occurrence of previous episodes, and previous hospital admissions. The only factor that did appear to interact with life events was maintenance chemotherapy: patients who had reduced or stopped medication showed no significant increase in life events immediately before relapse.

In the New Haven study (Jacobs & Myers, 1976), the results obtained were inconclusive, probably because the authors selected an over-long antecedent period (one year) for the comparison of event rates.

In the authors' view, the research carried out so far provides only provisional support for the hypothesis that life events are important in precipitating episodes of schizophrenia, and a replication of previous studies, using good methods of investigation, is overdue. Moreover, the relationship of life events to schizophrenia in cultures outside the Western world has been studied hardly at all. Ashour *et al* (1979) did examine life events in Egyptian schizophrenics, but the methodological idiosyncrasies of their study destroy their case for the role of stress in the onset of schizophrenia.

The current study of life events in the precipitation of episodes of schizophrenia among the people of the Najd area of Saudi Arabia uses methods based on those employed by Brown & Birley (1968). More details of our study, including a survey of the characteristics and culture of the Najd, have been provided by Al Khani (1983: unpublished doctoral thesis).

The Najd is a largely desert region, three times the size of France, which contains the Saudi capital, Riyadh. The society is a very traditional one which is now attempting to reconcile recent rapid development in material circumstances with the strict maintenance of Islamic values. The culture is very different from those of the developed world, particularly in terms of family life and the role of women. In the context of life-event research, it is likely that the impact of events is considerably modified by the prevailing attitude that circumstances arise primarily through the will of God, which must be accepted.

Our hypothesis was that life events would be significantly more frequent and have greater impact in the period immediately before episodes of schizophrenic illness than they would in the mentally healthy population of the Najd.

Method

The study was of a retrospective, case–control design. It involved a detailed assessment of selected schizophrenic patients attending various out-patient psychiatric clinics serving the area in order to discern the rate and impact of life events prior to the onset, relapse or exacerbation of schizophrenia. Similar assessments were made on mentally well individuals selected from the general population. The study was conducted between 20 December 1979 and 29 August 1981.

Instruments

The mental state of both controls and patients was assessed using the Present State Examination (PSE: Wing *et al*, 1974). This well-known semi-structured psychiatric interview consists of 140 items for which there is a glossary of differential definitions. The computer programs CATEGO and ID may be applied to the ratings from the interview. CATEGO provides a classification which, within limitations, may be seen as the equivalent of an ICD category (Wing, 1983). The ID (Index of Definition) program allocates subjects to one of eight levels which indicate the degree of confidence which can be placed upon the CATEGO class. Level 5, the 'threshold' level, has been used to distinguish 'cases' from 'non-cases' in the general population (e.g. Bebbington *et al*, 1981; Surtees *et al*, 1983), and in the current study control subjects were excluded if they were placed at this level or above. Before use, the PSE was translated into Arabic by Al Khani and his assistants, using several translations and back-translations after the manner of the IPSS (WHO, 1973).

For the recording of life events, there would have been considerable advantages in using the life-event interview and rating procedure developed by Brown & Harris (1978), but it was felt that such an open-ended approach would not be an effective way of eliciting information from Saudi subjects. We therefore adopted the (unpublished) WHO Life Events Schedule of 1978, which seemed to represent a happy compromise between Brown's approach and other more highly structured life-event inventories. The WHO schedule embodies a list of 70 specified events embedded in a structured interview which is intended to establish a narrative account of their timing and quality. The impact of the four most significant events is also rated.

One important methodological requirement was to ensure that events likely to have occurred as a consequence of the individual's mental state or behaviour were distinguished from those which occurred independently: an event in the first group could be the result of an emerging but sub-clinical psychiatric illness, rather than a precipitant of that illness. This problem was met in this study by classifying events into three categories:

1. *Uncontrollable events*—events which were apparently imposed on the subject and which for all practical purposes were outside his/her own control.
2. *Controllable/possibly-independent events*—events which lay within the subject's control, for which there was no evidence that they were associated with any behaviour exceeding the sanctions of the culture. Such events seem unlikely to have been effects of mental illness.
3. *Controllable/probably-dependent events*—events within the subject's control for which there was objective evidence to suggest that they might have been brought about by behaviour regarded locally as abnormal and possibly arising from the early stages of mental illness. Such events were excluded from analysis.

This classification of events represents a slight modification of the procedure advised in the WHO manual.

All the patients and controls, and at least one informant for each patient, were interviewed about the occurrence of life events. Events in the 12 months prior to the onset of schizophrenia or (for the control group) prior to interview were recorded.

Inter-rater reliability in the recording of life events was estimated with the help of Dr Al-Hamad, a Saudi psychiatrist. He studied the background of every subject in both groups without knowing whether a given subject was a patient or a control; he then studied in detail the narrative account of every scoring sheet and re-rated the presence/absence of every life event, the severity of its impact and its degree of independence. Inter-rater reliability was extremely good: agreement was 98% for presence of events and 94% for degree of independence. These results indicate that the schedule can be used satisfactorily in the Saudi cultural context.

Selection of subjects

Patients were selected from out-patient clinics serving the Najd area. To be included, patients had to be Saudis aged between 14 and 44, and to have lived with their families in the Najd area for at least one year preceding the onset of illness. Patients who had spent more than two of the last five years in a mental hospital were excluded, as were the mentally retarded and those with a history of alcohol or drug abuse or epilepsy. For each subject a complete physical examination and laboratory investigation was undertaken, to exclude those with endocrine, metabolic or nutritional disorders or acute or chronic brain syndrome.

When the acute disturbance of the index episode had settled, mental state was assessed using the PSE. We used an operational definition of schizophrenia, partly based upon the findings of the PSE, which depended on an evaluation of the following symptoms occurring in clear consciousness:

1. Subjective experience of disordered control of thought or body.
2. Persistent auditory hallucinations commenting on the patient or addressing him, not explicable in terms of depressed or elated mood.
3. Primary delusions and bizarre delusions.
4. Other delusions or hallucinations not congruent with depressed or elated mood.
5. Incongruous, blunted or labile affect.
6. Catatonic symptoms.

Patients with at least one symptom from the first three categories ('nuclear' symptoms) were classified as 'definite schizophrenics'. Patients without symptoms from any of the first three categories but with at least one symptom from the remaining categories were diagnosed as 'probable schizophrenics'. Both 'definite' and 'probable' schizophrenics were included in the study, provided the onset of the index episode had occurred within the previous three months and could be dated within a week. 'Onset' was defined as either the emergence of schizophrenic symptoms or an increase in their number or intensity. Onset in cases with previous symptoms was noticeably more difficult to determine: reliance had to be placed on previous case reports and interviews with relatives.

In addition to the operational definition of schizophrenia given above, and the CATEGO class, an ordinary clinical diagnosis was made using ICD categories. This took account of symptoms elicited by the PSE but also relied upon information about past episodes, overall course and premorbid personality.

The schizophrenic patients initially reviewed by Al Khani as potential subjects for the study numbered 112. Of these, 18 declined to take part and a further 43 did not meet the criteria for entry. The difficulty of finding subjects who met the stringent selection criteria and were willing to cooperate meant that it took more than 18 months to collect the 51 cases. While it may be argued that the final sample was not perfectly representative of Saudi schizophrenics, it did show considerable clinical similarities to groups with nuclear schizophrenia in industrialised societies.

The control group was obtained from the general population of the Najd area. No sampling frame giving a truly random sample is available, so they were selected at random from employees at King Saud University, from a school, the Educational College, and a village in the centre of the Najd, and also by approaching those who accompanied patients attending non-psychiatric out-patient clinics. Initially, Al Khani approached potential subjects and invited them to take part in a clinical interview: of 70 subjects thus approached, 36 refused to participate. Thereafter, the initial contact was made by handing the subjects a questionnaire based on the questions of the PSE; when this was returned they were invited to take part in a clinical interview. Although 9 subjects did not return the questionnaire, the 36 who did were obviously reassured by this procedure and agreed to an interview. The overall refusal rate of 39% could obviously have been much reduced if this tactic had been hit upon at an earlier stage.

The control subjects had to meet the same demographic criteria as the patient group. They also had to be mentally well, with no mental retardation and no history of psychotic illness, epilepsy, alcoholism or drug abuse. Their mental state was examined using a short Arabic version of the PSE, and the resulting data were submitted to the ID program. Of the 70 Saudis selected from the general population, eight subjects (11.4%) had symptoms which put them on or above level 5 of ID, and were therefore excluded. The remaining 62 formed the control group, and although they did not represent a random sample they were probably representative of the general population, with which they conformed in age, sex and marital status.

Analysis of data

The strategy of analysis was dictated by a desire to provide parallels with the studies of Brown & Birley (1968) and Jacobs & Myers (1976). Brown & Birley (1968) provided data on the three months before onset, broken down into four 3-week periods, and this procedure was also adopted here. However, we also considered longer antecedent periods in order to determine the time over which life events appeared to have an effect.

The analyses reported here were made on two different bases. First we compared the *frequency* of different categories of life events within different sub-groups. Secondly, we compared the *number of people* experiencing life events within different sub-groups. All the analyses were repeated with educational events excluded, as the timing of the Saudi academic programme led to a significant clustering of events in both male patients and male controls.

In this study, certain techniques of analysing the data have been used which although not novel in principle have not been used elsewhere in the life-event literature, at least not to the authors' knowledge. Previous studies of life events have relied on relatively simple statistics where they can be applied and on an intuitive appreciation of the data where they cannot. Our statistical techniques are justified at length in a paper still in preparation.

The data collected in this study were set out in two-dimensional contingency tables relating subject-group to life events in each of four 3-week antecedent periods. Each table was subjected to four types of analysis:

1. The distribution of events within each group was analysed separately to see if the frequency of life events differed with time: this can be termed *non-specific inhomogeneity*. This is an *exact* test to establish whether events tended to cluster in *any* of the four periods.
2. The distribution of events for each group was again analysed separately, to see if life events clustered in a *specific* period: any difference in the distribution of events between the last 3-week period and the mean of the other periods was tested for significance (*specific inhomogeneity*). This analysis yielded only an approximate value for probability.
3. We looked at differences between groups of subjects in the distribution of events over the four 3-week periods: different sub-groups of patients were tested against comparable sub-groups of controls.
4. Comparisons were made between the control subjects and different sub-groups of patients to see if there were significant differences between groups in the frequency of life events over the most recent 3-week period. This analysis used a permutational test.

While the first and second analyses were performed within groups, the third and fourth analyses compared groups. This strategy was needed to establish the significance of any differences between patients and controls and also to detect any patterns in the distribution of events within the patient group.

As statistical tests were applied to a large number of analyses, some apparently significant findings were likely to be type I errors. However, the relatively small numbers of patients and controls, especially in certain sub-groups, would tend in contrast to produce type II errors.

Results

Description of subjects

On the basis of PSE data and past history, 44 patients were given a clinical diagnosis of 'definite schizophrenia' and 7 'probable schizophrenia'. All cases of 'definite schizophrenia' fell into the CATEGO class S+ and the ICD9 equivalent 295.

Of the seven 'probable' cases, only two were classified as 'schizophrenia' by CATEGO. The diagnosis of a third was supported by the past mental history; the diagnosis of a fourth was supported by a subsequent relapse which included nuclear symptoms. The clinical diagnosis of the other three patients was at variance with the CATEGO classification and they were therefore excluded. The final study group therefore comprised 48 patients.

Table I describes the patient and control groups in terms of sex, age and marital status. Log linear analysis revealed a significant excess of males in the control group and unmarried subjects among the patients. These factors were controlled in the subsequent analyses.

Analysis of life events

These results are presented in greater detail by Al Khani (1983, unpublished doctoral thesis): we present here a selective summary. Where appropriate, tables give only those results significant at the 10% level. Absolute *P*-values are given to permit assessment of the strength of trends.

TABLE I
Age, sex and marital status of schizophrenic patients and controls

Sub-group	*Controls* ($n = 62$)	*Patients with no previous episodes* ($n = 21$)	*Patients with previous episodes* ($n = 27$)
Single males	22 (35%)	7 (33%)	11 (41%)
Single females	8 (13%)	6 (29%)	4 (15%)
Married males	16 (26%)	0	8 (30%)
Married females	16 (26%)	8 (38%)	4 (15%)
Males aged < 25 years	20 (32%)	6 (28%)	10 (37%)
Females aged < 25 years	15 (24%)	10 (47%)	2 (7%)
Males aged 25 or over	18 (29%)	1 (5%)	9 (33%)
Females aged 25 or over	9 (14%)	4 (19%)	6 (22%)
Mean age (years)	26.8	23.7	28.5

TABLE II

Six-month antecedent period: frequency of life events and number of subjects having at least one event, in different sub-groups of patients and controls

	Mean frequency of events		*Subjects having events*	
	Controls	*Patients*	*Controls*	*Patients*
Total group	1.44	1.94	71%	88%
Males	1.68	1.58	79%	85%
Females	1.04	2.36**	85%	91%
Married females	0.87	2.66*	75%	100%

* $P=0.02$, 1 d.f.

** $P=0.014$, 1 d.f.

No other significant differences between patients and controls

The frequency of life events in the control and patient groups over the six months before onset/relapse/interview is summarised in Table II. The frequency of events, especially uncontrollable events, was roughly equal in male patients and male controls. However, it was significantly higher in female patients than in female controls, especially in those patients with no previous history; and this was almost entirely due to events among married females. Analysis based on the number of subjects having events showed no significant differences between patients and controls. It is of interest in the Saudi context that male controls had a higher rate of events than females while the opposite was true for patients (Table II).

When the analyses were repeated with the antecedent period reduced to three months, frequency of events again appeared to be significantly associated with onset in females but not in males (Table III). The effect of events also appeared to be increased when the subject was married or the index episode was the first.

TABLE III

Three-month antecedent period: significance of life events (measured by mean frequency or by number of subjects with one or more events) for patients with and without previous episodes. P-values obtained by permutation tests

	Patients without previous episodes versus controls	*Patients with previous episodes versus controls*
Frequency of events		
Whole group	$P=0.022$	$P>0.1$
Females	$P=0.011$	$P=0.062$
Married females	$P=0.036$	$P=0.041$
Number of subjects with events		
Whole group	$P=0.0075$	$P>0.1$
Females	$P=0.091$	$P>0.1$
Married females	$P=0.027$	$P>0.1$

We then divided the 3-month period before onset into four 3-week sections. This corresponds to the framework used by Brown & Birley (1968), and in Table IV their results are compared with those of the current study. The increase in the frequency of life events in the last 3-week period in the Saudi group as a whole failed to reach significance at the 5% level. However, it seemed possible that this result disguised significant effects in particular groups, so the pattern of events was examined further.

TABLE IV

Percentage of subjects experiencing independent or possibly independent life events in the three months before onset: comparison of the Camberwell study (Brown & Birley, 1968) and the present study

	3-week period			
	1st	*2nd*	*3rd*	*Last*
Camberwell				
Patients	30	18	20	60
Controls	21	20	18	19
Najd				
Patients	19	17	19	31
Controls	21	21	13	16

The results for the *control subjects* are summarised in Table V. Analysis involved examination of the number of events experienced in a group. In male controls, there appeared to be a departure from the random distribution of events, giving a significant result for non-specific inhomogeneity ($P=0.027$). However, this was wholly due to those who were single, and was attributable solely to educational events: the effect disappeared when these were excluded. The pattern of these findings was repeated when analyses were based on the percentage of subjects having events: i.e. there were no specific inhomogeneities in the controls, which is of course as it should be. All the analyses reported below were repeated with educational events eliminated. This made no noticeable difference to the findings.

It was found that for *patients in their first episode* (Table VI) there was a significant specific inhomogeneity for women, i.e. events tended to cluster in the three weeks before onset. This was mostly due to events among the married women, and was reflected in the figures for the whole group. When these analyses were repeated on the basis of the number of patients with events, similar results emerged (Table VI). Among patients who *had* suffered

TABLE V

Analysis for non-specific inhomogeneity in life events of control subjects (measured by frequency of events or by number of subjects with one or more events). The three months before interview were sub-divided into four 3-week periods. A low P-value implies a non-random, non-homogeneous distribution

Basis of analysis	*Number in each 3-week period* *1st*	*2nd*	*3rd*	*Last*	*Results of exact test (3 d.f.)*
Frequency of events	*Number of events*				
All events: males ($n=38$)	10	13	2	9	$\chi^2=9.54$; $P=0.027$
All events: single males ($n=22$)	6	10	1	3	$\chi^2=9.77$; $P=0.025$
Controllable/possibly independent events: total group ($n=62$)	8	8	2	2	$\chi^2=7.71$; $P=0.061$
Controllable/possibly independent events: males ($n=38$)	6	7	0	2	$\chi^2=11.86$; $P=0.011$
Controllable/possibly independent events: single males ($n=22$)	5	5	0	0	$\chi^2=13.86$; $P=0.0054$
Numbers of subjects with events	*Number of subjects*				
Males ($n=38$)	9	11	2	8	$\chi^2=7.45$; $P=0.067$
Single males ($n=22$)	5	8	1	3	$\chi^2=6.76$; $P=0.078$

TABLE VI

Analysis for specific inhomogeneity in life events of patients with no previous episodes of schizophrenia. The last 3-week period before onset was compared with the previous 9 weeks

Basis of analysis	*Number in each 3-week period* *1st*	*2nd*	*3rd*	*Last*	*Results of approx. test (1 d.f.)*
Frequency of events	*Number of events*				
All events: total group ($n=21$)	4	5	5	12	$\chi^2=5.44$; $P=0.020$
All events: females ($n=14$)	2	3	5	10	$\chi^2=5.57$; $P=0.016$
All events: married females ($n=8$)	1	2	3	7	$\chi^2=4.91$; $P=0.027$
Uncontrollable events: total group ($n=21$)	2	2	3	9	$\chi^2=7.05$; $P=0.0079$
Uncontrollable events: married females ($n=8$)	0	1	1	5	$\chi^2=6.64$; $P=0.01$
Numbers of subjects with events	*Number of subjects*				
Total group ($n=21$)	4	4	3	9	$\chi^2=3.76$; $P=0.053$
Females ($n=14$)	2	3	3	7	$\chi^2=3.28$; $P=0.070$
Married females ($n=8$)	1	2	2	5	$\chi^2=2.88$; $P=0.09$

earlier episodes (Table VII) there was significant evidence of specific inhomogeneities only among married women, although the effect was reflected in the group as a whole. Further analysis based on the number of patients having events confirmed this result.

This analysis of the pattern of events within each group is purely suggestive, although of course it can be seen as quite important that the inhomogeneities in the control groups were random, while those in patients were due to clustering immediately before onset. However, the crucial test of the hypothesis that life events are significantly associated with the onset of schizophrenia is the comparison of patients with controls, which was done firstly by comparing the patterns of distribution of events over the four 3-week periods, and secondly by examining the frequency of events in the 3-week period immediately before onset.

When the overall patterns between groups were compared we were surprised to find that the only significant findings appeared in the comparison of controls with patients *who had experienced previous episodes* (Table VIII). This result was largely due to the results for married women.

Significant differences between controls and patients

TABLE VII

Analysis for specific inhomogeneity in life events of patients with previous episodes of schizophrenia. The last 3-week period before onset was compared with the previous 9 weeks

	Number in each 3-week period				*Results of approx. test (1 d.f.)*
Basis of analysis	*1st*	*2nd*	*3rd*	*Last*	
Frequency of events		*Number of events*			
All events: married females ($n=4$)	1	0	0	5	$\chi^2=9.03$; $P=0.0027$
Controllable/possibly independent events: total group ($n=27$)	1	1	1	5	$\chi^2=5.00$; $P=0.025$
Controllable/possibly independent events: married females ($n=4$)	0	0	0	3	$\chi^2=4.39$; $P=0.039$
Numbers of subjects with events		*Number of subjects*			
Married females ($n=4$)	3	0	0	1	$\chi^2=4.39$; $P=0.036$

TABLE VIII

Differences in the pattern of life events over 3 months for controls and patients with previous episodes

	Number in each 3-week period				*Interaction between patterns of distribution*
Basis of analysis	*1st*	*2nd*	*3rd*	*Last*	
Number of events: males					
Controls ($n=38$)	10	13	2	9	$\chi^2=3.30$; $P=0.098$
Patients ($n=19$)	5	3	5	3	
Number of events: married females					
Controls ($n=16$)	2	2	3	1	$\chi^2=11.23$; $P=0.027$
Patients ($n=4$)	1	0	0	5	
Number of uncontrollable events: single males					
Controls ($n=22$)	1	5	1	3	$\chi^2=7.45$; $P=0.059$
Patients ($n=11$)	1	0	2	0	
Number of controllable/possibly-independent events: total group					
Controls ($n=62$)	8	8	2	2	$\chi^2=8.75$; $P=0.033$
Patients ($n=27$)	1	1	1	5	
Number of controllable/possibly-independent events: females					
Controls ($n=24$)	2	1	2	0	$\chi^2=10.59$; $P=0.014$
Patients ($n=8$)	0	0	0	3	
Number of controllable/possibly-independent events: married females					
Controls ($n=16$)	1	1	1	0	$\chi^2=8.32$; $P=0.040$
Patients ($n=4$)	0	0	0	3	
Number of subjects having events: married females					
Controls ($n=16$)	2	2	3	1	$\chi^2=0.77$; $P=0.019$
Patients ($n=4$)	1	0	0	3	

were more in evidence when direct comparisons were made of events in the 3-week antecedent period (Table IX). For those who had suffered earlier episodes, significant findings were confined to females: this was largely due to a marked increase in frequency of events among married women. For patients in their first episode, significant findings were against restricted to females, but an increased frequency of events was seen in both single and married women.

In the study of Brown & Birley (1968), the authors provided tentative evidence that schizophrenic relapse often occurs in response not to a single event but to an accumulation of events. Their argument was based on the finding that 70% of patients with a life event in the three

TABLE IX

Comparisons of life events of patients and controls over a 3-week antecedent period, using a permutation test. Each sub-group of patients was compared with the equivalent sub-group of controls

Basis of analysis	*Patients with previous episodes*	*Patients with no previous episodes*
Number of events: total group	$P>0.1$	$P=0.022$
Number of events: females	$P=0.062$	$P=0.011$
Number of events: married females	$P=0.012$	$P=0.005$
Number of subjects having events: total group	$P>0.1$	$P=0.029$
Number of subjects having events: females	$P>0.1$	$P=0.0075$
Number of subjects having events: married females	$P=0.022$	$P=0.016$
Number of uncontrollable events: females	$P>0.1$	$P=0.050$
Number of controllable/possibly-independent events: total group	$P=0.014$	$P=0.030$
Number of controllable/possibly-independent events: married females	$P=0.061$	$P>0.1$

weeks before onset also reported events in an earlier period: in contrast, only 35% of patients with no life events in the three weeks beforehand reported events in earlier periods. It was thought worthwhile to repeat this analysis in the current study; but where Brown & Birley (1968) obtained figures of 70% and 35%, we obtained 33% and 41%. Our study thus provides no evidence for an additive effect of events.

Discussion

The current study and that of Brown & Birley (1968) both relied on the PSE to elicit symptoms, although different editions were used. There were also some differences between the clinical criteria for inclusion in the present study and those used by Brown & Birley: they included delusions of reference, delusions of persecution and grandiose, religious and somatic delusions as symptoms implying definite schizophrenia and qualifying the case for inclusion. In the present study, these symptoms were regarded as indicating 'probable schizophrenia': the presence of one of them was not by itself sufficient to justify inclusion of the case. Our criteria were designed to select only unequivocal cases of schizophrenia despite the cultural context. Our sample therefore differed from the London sample of Brown & Birley (1968) in not including non-nuclear paranoid psychoses, but there is no reason to suppose that these differences in symptoms should lead to different relationships between events and onset, especially as the samples comprised similarly acute cases and contained a roughly similar proportion of first episodes. Criteria for onset were identical in the two studies.

The control group in our study was representative rather than random, but this was also true of the London study, in which the 325 controls were derived from the employees of local firms. In our study the method of eliciting life events was based on the WHO Life Events Schedule, which is derived from Brown's schedule. Further detailed comparison of the studies is given in Table X. All things considered, the methods used in this project were sufficiently similar to the methods employed by Brown & Birley (1968) for it to be regarded as a replication of their study.

In the current study, we included for analysis events in the categories 'uncontrollable' *and* 'controllable/possibly independent'. This was probably an adequately conservative decision, which still yielded a reasonably accurate estimate of the role of life events in precipitating episodes of schizophrenia. Overall, it seems improbable that the imperfections of the study led to any systematic bias: they would if anything have operated as random noise, which would have reduced the chance of significant positive findings.

In the event, the results of the study are equivocal. The frequency of life events in the patient group over the six months before onset, although higher than that among controls, was not significantly so. Female patients *did* have a significantly higher rate of life events than female controls, and this was mostly attributable to those who were married. This

TABLE X

Comparison of the samples in this study of the Najd population and the London study of Brown & Birley (1968)

	London		*Najd*	
	Patients	*Controls*	*Patients*	*Controls*
Number	$n=50$	$n=325$	$n=48$	$n=62$
Sex	48% male 52% female	40% male 60% female	54% male 46% female	61% male 39% female
Marital status:				
Single	62%	46%	58%	48%
Ever married	38%	54%	42%	52%
Previous psychiatric history	30%		56%	
Diagnosis:				
d. Definite schizophrenia	*d* 48% definite		*d* 92% definite	
p. Probable schizophrenia	*p* 52% probable		*p* 8% probable	
Type of onset:				
Previously normal	*d* 22% *p* 36%		*d* 40% *p* 4%	
Non-schizophrenic psychiatric symptoms turning to schizophrenia	16%		35%	
Mild schizophrenic symptoms becoming more severe	26%		21%	
Mean age	33.80 years (*d* 38.2) (*p* 29.3)	32.72 years	25.8 years	26.8 years

pattern became much more apparent as the period analysed was progressively shortened.

In patients who had experienced previous episodes, the findings for married women stand in marked contrast to those of all other groups, in which there was no detectable increase in the number of events before onset whatever the period of analysis. Male patients and single female patients in their first episode of schizophrenia did show an increased frequency of events in the three weeks before onset, but this did not reach acceptable levels of statistical significance.

The discrepancies between these results and those of Brown & Birley (1968) require careful consideration. The first possible explanation is that our findings relating to married women arise through chance or artefact, the true state of affairs being that life events do not provoke the onset of schizophrenia. If this were so, it would be hard to argue the case for *any* psychosocial stressor having an important effect on onset or relapse in schizophrenia. Life events represent a substantial sample of the domain of psychosocial stress, and if psychosocial stress is important one can reasonably expect this importance to be revealed in an association between life events and onset.

A less extreme explanation is that the association between life events and onset exists but is weak, and that the discrepancy between the results of the Brown & Birley study and the present work arose through sampling differences. However, the finding among married women of a marked and suggestive rise in frequency of life events immediately before onset is difficult to discount.

If our results are accepted at face value, consideration must be given to the explanation of the negative results in certain sub-groups. These could have arisen because of chance peculiarities in either the patient group or the control group: methodological defects, in contrast, would have been more likely to operate on the study as a whole. Another possibility is that the negative results occurred because those particular groups of patients were exposed to some source of psychosocial stress not covered by the rubric of a life-event list. Such possible sources include family atmosphere and the rapid cultural change occurring in Saudi Arabia. Leff *et al* (1983) have recently claimed that life events and a poor family atmosphere (as reflected in Expressed Emotion—EE) can operate as alternatives in this way. The intrusiveness and stressfulness of family life are generally considered to be less in non-Western than in Western societies (Leff, 1981, p. 156); Wig & Menon (1985) have provided evidence that this is so in India. Whether the superficially similar family circumstances prevalent in Saudi Arabia are also associated with low stress is not yet known.

There is no doubt that Saudi Arabia is experiencing rapid cultural change, and if this did operate as a significant source of psychosocial stress the findings of the current study would be less unexpected. While the opportunities now available to women in Saudi Arabia represent a radical break with tradition, they are as yet being taken up only by a few: it is thus the men who are more exposed to the effects of change in the society.

One further factor which is likely to influence the impact of life events on psychiatric disorders in Saudi Arabia is locus of control (Rotter, 1966). The culture of Saudi Arabia, as with many Muslim countries, inclines towards an external locus of control in the form of a belief in the over-riding influence of Allah and the importance of submitting to his will. This contrasts sharply with the cult of individual effectiveness found in Western societies (e.g. Husaini & Neff, 1980). Where an external locus is the norm, it is not clear what its effect is or how individual variations in locus of control affect susceptibility to life events, but research into these effects in a Saudi context might elucidate the whole topic of the psychological moderation of the impact of life events.

The most likely interpretation of the results from this study is that in Saudi Arabia, as in the West, episodes of schizophrenia in certain people are preceded by life events which have a genuine role in precipitating them. The theoretical interest of the study is that it adds to a growing impression that although life events operate as precipitants in schizophrenia, they do so because they are a sample of a larger domain of potentially upsetting social circumstances.

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M. A. F. Al Khani, MD, PhD, *Assistant Professor in Psychiatry, Medical College, King Saud University, PO Box 15102, Riyadh, Saudi Arabia*

*P. E. Bebbington, MA, MPhil, MRCP, MRCPsych, *Hon. Senior Lecturer, MRC Social Psychiatry Unit, Institute of Psychiatry, De Crespigny Park, London SE5 8AF*

J. P. Watson, MD, FRCP, FRCPsych, *Professor of Psychiatry, United Medical Schools (Guy's Campus), London SE1 9RT*

F. House, DipTech, MSc, PhD, *Senior Lecturer, Department of Pharmacology, United Medical Schools (Guy's Campus), London SE1 9RT*

*Correspondence

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A Validity Study of a Psychiatric Screening Questionnaire (SRQ-20) in Primary Care in the city of Sao Paulo

JAIR de JESUS MARI and PAUL WILLIAMS

A validity study of the Self-Report Questionnaire (20 item version, Harding *et al*, 1980) against the criterion of a standardised psychiatric interview (Goldberg *et al*, 1970) was carried out at three primary care clinics in Sao Paulo; 875 patients filled in the SRQ-20 questionnaires and a subsample of 260 was interviewed by the psychiatrist. The SRQ-20 was shown to be a feasible screening instrument for psycho-emotional disturbance in these settings. Sensitivity was 83% and specificity 80%, and the questionnaire was a good indicator of morbidity. A correlation was found between questionnaire total scores and independent clinical judgment (r = +0.70). A sex difference in the validity coefficients is described.

The Self-Report Questionnaire (SRQ) is an instrument which was designed to screen for psychiatric disturbance in primary care settings. It was derived from four previously developed psychiatric research instruments for use in the WHO study of psychiatric morbidity in primary care settings in developing countries (Harding *et al* 1980, 1983). In Brazil, it has been used by Busnello *et al* (1983) in a primary care setting in Pôrto Alegre, but validation results from this study have not yet been published. This present investigation is an attempt to assess the feasibility and validity of the SRQ-20 as a screening questionnaire for psycho-emotional disturbance in primary care clinics in Brazil.

Method

Instruments

The Self-Report Questionnaire (SRQ; Harding *et al* 1980) comprises 24 items, which are divided into two sections. The first 20 items are designed to detect non-psychotic disorders, and the remaining four intended to screen for psychotic disturbance. The items were selected by Harding *et al* (1980) from previously developed psychiatric screening instruments in use in four different countries (the P.A.S.S.R. from Colombia [Climent & Plutchik, 1980]; the P.G.I., from India [Verma & Wig, 1977]; the G.H.Q. from Great Britain [Goldberg 1972] and the shortened version of the P.S.E., also from Great Britain [Wing *et al* 1974]). The present study was carried out in a primary care setting, so that it was decided to use the 20-item version, i.e. that section of the instrument concerned with non-psychotic symptoms.

The Clinical Interview Schedule (C.I.S.—Goldberg *et al* 1970) is a semi-structured psychiatric interview, which was designed to study non-psychotic disorders in extramural settings. It has been widely applied in general practice, and its feasibility in this setting has been tested in a number of different countries (e.g. Goldberg & Blackwell 1970; Tennant 1977; Munoz *et al* 1979; Dhadphale *et al* 1983). It is divided into four sections, containing ratings based on symptoms reported by the patient (arranged in ten groups) and 12 items that represent the psychiatrist's view of the 'manifest abnormalities'. These and a global clinical psychiatric rating are rated by the psychiatrist, using five-point scales. Respondents can be classified as 'case' or 'non-case' on the basis of the total weighted score (see Goldberg *et al* 1970 for details of the scoring method).

A Portuguese translation of the C.I.S. is available. It has been applied in a pilot study in Brazil, and has been found to be feasible and reliable for use in primary care settings in that country (Mari & Williams 1983, 1984).

Procedure

The study was conducted in three primary care units in the city of Sao Paulo. Two were health centres (Ladeira Rosa and Bom Retiro/Barra Funda), and the third was an outpatient clinic (providing primary rather than secondary care) in a general hospital (Hospital do Servidor Público Estadual de Sao Paulo).

A time-sample of attenders aged 16 or more at each of these three clinics was asked to fill in the Self-Report Questionnaire (SRQ-20) and the General Health Questionnaire (GHQ-12), before seeing the general physician (results pertaining to the GHQ-12, and a comparison of the SRQ-20 and the GHQ-12, will be published elsewhere). As far as possible, each of the primary care units was sampled (on randomly-selected days) twice each week. On the selected day, the unit was visited by the psychiatric research worker (JM) and his assistant. On the basis of the pilot study (Mari & Williams, 1984) it was decided that the research assistant would read the questions to those patients who had less than eight years of formal education.

The patients were then classified into two groups, according to their GHQ scores (low, 0–3; high, 4+). Then, the research assistant randomly selected one low and one high scorer from each session for interview by the psychiatrist. The psychiatric interview was conducted blind, without knowledge of the questionnaire results.

Results

The sample

Data were collected simultaneously in the three primary care clinics from September 1983 to February 1984; 875 patients completed the SRQ and 260 were interviewed. Eight patients were not included because of their physical condition, and three refused the psychiatric interview. There were no significant differences between the total sample and the interviewed sub-sample in sex ratio, marital status, educational level or family income. Thus, the sample selected for interview can be regarded as representative of the patients attending the three primary care clinics.

The SRQ-20 as a screening instrument

Completing the questionnaire took roughly five minutes, and the questions were easily understood by the patients.

Figure 1 shows values for sensitivity and specificity (weighted estimates calculated according to the procedure of Diamond & Lilienfeld [1962] so as to apply to the total sample) for a variety of values for the case/non-case threshold. It can be seen that the best value—i.e. the best 'trade off' between sensitivity and specificity—was found to be 7/8. Using this threshold, the sensitivity and specificity were found to be 83% and 80% respectively. The positive and negative predictive values were both 82%, and the overall mis-classification rate was 18%.

Similar calculations were carried out for sub-groups defined according to each of the socio-demographic characteristics (age, sex, marital status, race, educational level, and family income). The validation results were not affected by age, marital status, race, educational level, or income. However, it was found that the best cut-off point for the males was 5/6 (sensitivity 89% and specificity 81%), whereas for the females it was 7/8 (sensitivity 86% and specificity 77%). Using 7/8 as the threshold, the positive predictive value was markedly lower for the men (66%) than for the women (83%), although this difference was not statistically significant ($\chi^2 = 2.18$, 1 d.f.).

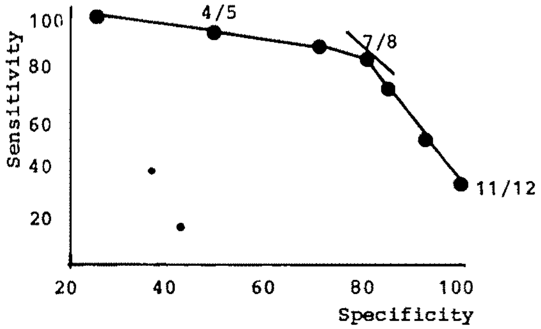

FIG. 1 The relationship of sensitivity to specificity of the SRQ-20 using different cut-off points for the total sample.

The SRQ as an indicator of morbidity

To evaluate the SRQ as an indicator of morbidity, respondents were classified as high ($\geqslant 8$) or low ($\leqslant 7$) scorers. Then, the mean scores of the two groups for the items in the Clinical Interview Schedule wre compared. The results are shown in Figure 2.

The differences between sample means were statistically significant ($p<0.01$) for *all* the 'reported symptoms' of the interview, and for the 'manifest abnormalities' histrionic, depressed, anxious/agitated, excessive concern with bodily functions, and depressive thoughts. The remaining seven manifest abnormalities occurred so infrequently as to render comparison impossible and meaningless.

The SRQ as an indicator of severity

To assess whether the SRQ-20 score was correlated with the severity of symptoms, as assessed by the psychiatrist, correlation coefficients between the SRQ scores and the ratings obtained in the psychiatric interview were calculated. There was a strong correlation between the total

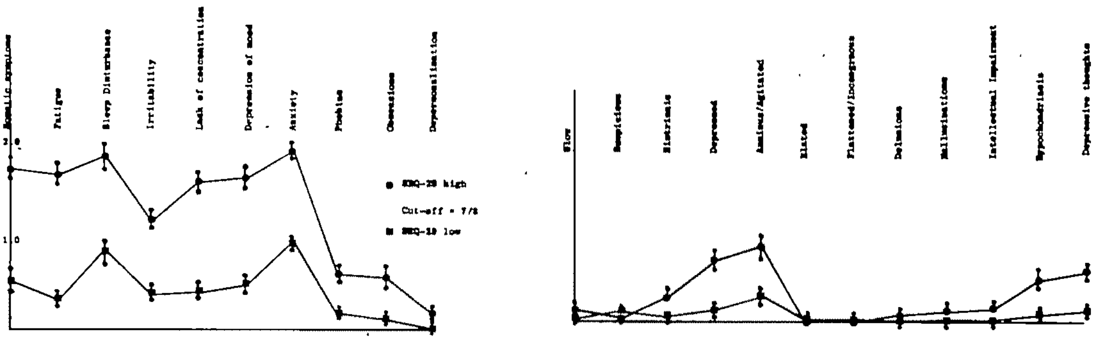

FIG. 2 The mean score of individual items reported in the psychiatric interview for high and low SRQ-20 scorers.

SRQ-20 score and the overall clinical assessment made by the psychiatrist (r = +0.70), the total weighted score (r = +0.74), and the reported symptom score (r = +0.75). The correlation was less strong (r = +0.55) when the SRQ scores were compared with ratings of the manifest abnormalities in the CIS.

Discussion

The SRQ was first applied by Harding *et al* (1980), in a study set up by W.H.O. to investigate mental illness in four developing countries (Colombia, India, Sudan, and the Phillipines). The performance of the SRQ was then assessed against the P.S.E. (Wing *et al*, 1974), and the validation results were reported to be as follows:

sensitivity	73%–83%
specificity	72%–85%
misclassifcation rate	18%–24%

The SRQ has also been applied in Brazil by Busnello *et al* (1983) to 242 primary care attenders, but validation coefficients have not been reported.

Dhadphale *et al* (1983) conducted a validation study of the S.R.Q. in Kenya against the C.I.S.: 61 psychiatric clinic patients were compared with 65 controls matched for age, sex, and education. The specificity reported was ">93.3%" and the sensitivity was 89.2%.

The validation coefficients obtained in the present survey are intermediate between those reported by Harding *et al* (1980) and by Dhadphale *et al* (1983). However, it is important to consider some methodological limitations in the studies described. Harding *et al* used the PSE as the validating interview, and there are grounds for suspecting that instruments like the PSE, that have been developed on and primarily for psychiatric patient samples, may not be the most appropriate for community and primary care settings (Dohrenwend *et al* 1978, Duncan-Jones & Henderson 1978, Williams *et al* 1980a,b, Busnello *et al* 1983).

Also, Harding *et al* (1980) applied the psychiatric interview to a highly skewed sub-sample of respondents (90% of high SRQ scorers and only 10% of low scorers). It is not clear whether the validity coefficients were subsequently adjusted so as to be representative of the screened sample as a whole (Diamond & Lilienfeld, 1962)—an adjustment which is crucial. Similarly, it is not clear whether the coefficients reported by Dhadphale *et al* (1983) were adjusted in a like manner. Also, in their study (which yielded very high values for the validity coefficients), known patients were compared with known normals—a situation likely to minimise misclassification. As Williams *et al* (1980a) observe, "instruments which can distinguish clearly between distinct caseness groups, i.e. well separated locations on the continuum (of illness), need not necessarily perform well in classifying individuals of varying and intermediate probabilities of illness". It is also relevant to note that neither of these studies quote predictive values.

Broadly speaking, the validity coefficients were not affected by the socio-demographc variables. There were no statistically significant relationships, but for practical reasons, a different cut-off point of this instrument for each sex (5/6 male, 7/8 female) might be considered. This finding (a higher false negative rate in men than in women) could be related to possible sex differences in illness behaviour (Mechanic, 1977). Briscoe (1982) has also pointed out that the expression of emotion would be more stigmatising for men. However, further investigation on this matter should be carried out before reaching a final conclusion.

The present study also found that the SRQ-20 was acceptable as an indicator of morbidity and at a population level (but not necessarily at an individual level), acceptable as a measure of severity.

The results of this study suggest that the SRQ-20, in conjunction with an appropriately translated version of the C.I.S., is appropriate for use in two-stage screening surveys in primary care settings in developing countries. However, further research on the use of screening instruments in such settings is required. In particular, work might usefully be directed towards investigating the differential effect of social and demographic factors on validity.

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*Jair de Jesus Mari, MD, *Lecturer in Epidemiology & Psychiatry, Department of Social Medicine, Faculty of Medicine, Santa Casa of Sao Paulo, Brazil.*

Paul Williams, MB, MRCPsych, *Senior Lecturer, General Practice Research Unit, Institute of Psychiatry.*

*Correspondence: Dr. Jair de Jesus Mari, *Research Worker, General Practice Research Unit, Institute of Psychiatry, London SE5.*

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A Baseline Study on Mental Disorders in Guiné-Bissau

JOOP T. V. M. DE JONG, GUUS A. J. DE KLEIN and SINEKE G. H. H. M. TEN HORN

Adults attending general health facilities in Guiné-Bissau were screened for the presence of mental disorder; minimum estimate of definite mentally ill cases was found to be 12%. The proportion correctly identified by general health workers was low: only one of every three patients with a mental disorder was recognised and of every 100 non-cases 12 patients were wrongly diagnosed by the health worker as suffering from psychiatric illness. On the basis of these results health workers are now being taught how to detect mental illness.

Advances in techniques of reliable case detection (Goldberg, 1974) have resulted in a number of studies showing that psychiatric disorders, and especially non-psychotic illnesses, are among the most common reasons for which doctors are consulted (Dilling *et al*, 1978; Hoeper, 1979; Marks *et al*, 1979). Goldberg & Blackwell (1970) found conspicious psychiatric morbidity in a London general practice to be about 20%, while Giel (1972) stated that mental illness, as diagnosed by a psychiatrist in a random sample of subjects aged 15 years or over in a Dutch village, amounted to 13%. It might be expected that in developing countries fewer patients with psychiatric disorders contact the primary health care facilities, either because the proper diagnosis cannot be made by the workers with less comprehensive training or because mental disorders are overshadowed by physical ones such as malnutrition or infectious and parasitic diseases. However, some studies show that the number of cases of psychiatric disorder seen in primary health care may in fact be similar in developing countries to those elsewhere (Dormaar *et al*, 1974; Giel & Van Luijk, 1969; Mbanefo, 1971; Harding, 1973; Ndetei & Muhangi, 1979). For example, in the WHO Collaborative Study on Strategies for Extending Mental Health Care in four developing countries, the recorded frequency of psychiatric disorders—between 10.6 and 17.7%—was just below the percentages found in industrialised countries (Harding *et al*, 1980).

The purpose of this study was to develop and evaluate low-cost methods for mental health care, to determine treatment priorities within the framework of a general health service in Guiné-Bissau. After completion of the baseline study, the health workers are to receive brief, task-oriented training on the detection and management of a limited number of priority psychiatric disorders, and the results of this training will be evaluated by subsequent observations.

In this paper, part of the baseline study is reported. Adult patients attending general health facilities were screened for the presence of psychiatric disorder, and the proportion correctly identified by the general health workers was established. Data about the screening of children will be published elsewhere, as well as the results of the structured questionnaire administered to groups of key informants and general health workers in the study area.

Guiné-Bissau is about the size of Switzerland, with 850,000 inhabitants. After independence in 1974, at the end of 13 years of fighting, the health authorities, recognising a lack of mental health facilities (apart from two old custodial wards), accepted a mental health policy with three priorities (De Jong, 1982, 1983): firstly, to deliver mental health care with a focus on the rural areas; secondly, to develop an ambulatory social psychiatric team to make regular visits to the major hospitals in the country; and thirdly, to improve institutional psychiatric care by building and organising a small socially integrated psychiatric clinic, operating in line with current ideas.

Method

The population

We selected our study area by two criteria. The first was that it should have an average socio-economic level, and the second that some people in the area should have participated in the fighting (to find out if some mental health problems could be attributed to this war). The selected area in southern Guiné-Bissau meets these criteria; it is less wealthy than parts of the North, and more developed than the East, but representative of rural Africa. During the war, some people in this part of the country remained under Portugese rule whereas others did not.

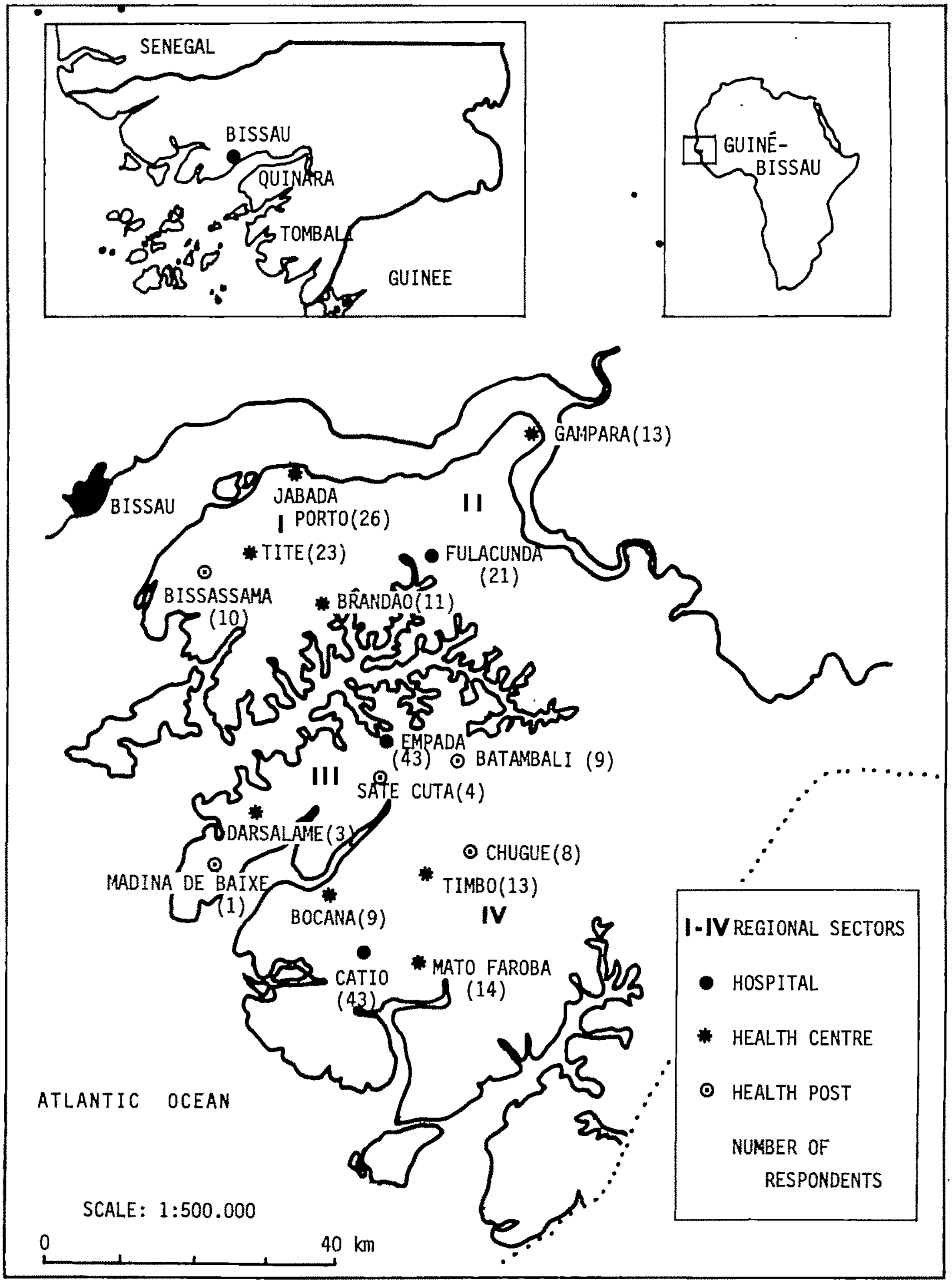

FIG. 1 Distribution of Health Institutions in the Study Area and the Number of Respondents per Institution.

There are 37 sectors in Guiné-Bissau. The four southern ones, which we studied, are situated in a flat coastal area, dissected by innumerable sea arms. The higher areas are covered by tropical forests, whereas the mainly agricultural population cultivating rice or millet, is concentrated along the sea arms. These crops, animal husbandry, and fishing are mainly for their own consumption. The area has 41,850 people, with a density of 13 per square kilometre. A few hundred villages, each with a small number of inhabitants, are clustered closely together; during the rainy season, most can be reached only by foot, landrover, or motor-cycle. Some small cities lie along the main road and public transport passes through this area only once or twice a day. About 5% of the population has running water or electricity for a couple of hours every day; 70% gets its water from a covered well; the others use open wells or ponds near their homes. Houses are built from mud and covered with a thatched roof; 90% of the population has no formal education. The group we studied lives with no notion of today's outside world: half of them do not know their age, the date or year in which we are living, or the name of their president. Three-quarters of the studied group possess rice fields, which provides enough rice for half of them. The principal endemic diseases in the area are malaria, respiratory infections, diarrhoea, skin diseases, wounds, and tuberculosis. Principal causes of death are malaria, respiratory diseases, and tetanus; infant mortality is above 20%.

Since Independence, the government has succeeded in building up a pyramidal health structure in the rural areas. This consists of a pilot primary health care project in the South of the study area, with participating villagers trained on the spot; beyond this, there is a network of health posts, health centres, and three hospitals. In sector I, there is no hospital, but three health centres and one health post; in sector II, there is one hospital and one health centre, but no health post; in the third and fourth sectors, all three types of facilities are available.

Patient-selection

A list of all health facilities in the area, together with the average weekly number of consultations given to adult patients in each facility, was drawn up. As there were no data available for one of the sectors and inconsistent ones on the others, we collected data ourselves over two successive three-month periods. Because drugs are distributed quarterly, there is a sharp increase in consultations during the first month following distribution, followed by a decline close to zero in the third month. To acquire statistically significant data, we fixed the number of adults to be screened at 300 per 50,000 inhabitants which yielded 252 respondents; the number of people to be screened was set for each health facility in proportion to the attendance rates. Next we carried out screening in turn at each facility. Patients were inspected in five health posts, eight health centres, and the three hospitals. Whenever possible, no warning to the staff of the health facility was given about the screening until the evening before, to prevent special selection of patients. Screening always started with the first patient aged 16 years or older, attending in the morning. We excluded patients who were so seriously ill that it would have been insensitive to give questionnaires. Consecutive attenders, if necessary on more than one day, were screened until the number set for the facility was reached. No patient refused to take part.

Basic identifying data and a number of socio-demographic data were obtained on each patient. We asked why they had come to the health facility, the response being recorded verbatim. The screening process was carried out independently of the consultation or treatment process. No health worker who was seeing the patient had access to the results of the inquiry. Each health worker indicated at the end of the normal consultation process, by marking a cross on the Health Staff Rating Schedule (HSR), whether or not he thought mental disorder was indicated, alone or in combination with a physical health

TABLE I

Diagnoses of psychiatric disorders seen in primary health care: of the 57 patients followed up and identified (PSE) as 'possible' or 'definite' cases

		'possible'		*'definite'*		*'pos + def'*		*Harding*
		abs	*(%)*	*abs*	*(%)*	*abs*	*(%)*	et al *(1980)*
Depressive neurosis	(300.4)	4	(33.3)	12	(52.2)	16	(45.7)	48.6%
Hysteria	(300.1)	—	(8.3)	3	(17.4)	3	(14.3)	8.3%
Hypochondriasis	(300.7)	1		1		2		
Anxiety neurosis	(300.0)	—	(0.0)	1	(4.3)	1	(2.9)	30.9%
Unspecified psychosis	(298.9)	4	(33.3)	—	(4.3)	4	(14.3)	3.1%
Psychogenic par. psych.	(298.4)	—		1		1		
Schizophrenia	(295)	—		—		—		
Affective psychosis	(296)	—	(0.0)	1	(4.3)	1	(2.9)	1.7%
Prolonged depres. reac.	(309.1)	—	(25.0)	1	(17.4)	1	(20.0)	7.3%
Par. personality dis.	(301.0)	1		—		1		
Alcoholic hallucin.	(291.3)	—		1		1		
Generalised convulsive epilepsy	(345.1)	—		2		2		
Others		2		—		2		
Total		12	(100.0)	23	(100.0)	35	(100.0)	100.0%

problem, or if no health problem of any kind could be diagnosed. Comparison between the health workers' ratings and the diagnoses given by the research psychiatrist can be calculated in two different ways. The first is the diagnostic sensitivity, defined as a measure of how few cases are missed, by dividing the total number of 'cases' detected by the health worker and those also identified as such by the research psychiatrist, with the total number of cases identified at follow up. Secondly, there is the diagnostic specificity, a measure of how few non-cases are diagnosed as cases by the health staff worker, by dividing the total number of non-cases identified by him and by the research psychiatrist by the total number of non-cases at follow-up.

First-stage screening

We used a self reporting questionnaire (SRQ) with 26 questions, of which the first 20 were constructed to detect non-psychotic disorders. Four additional questions were to detect psychotic conditions, and two more were added, one for epileptic or other fits and one for alcoholism. The design of the SRQ is based on a concensus among the investigators of the WHO Collaborative Study (Harding *et al*, 1980). We used the Portuguese version, prepared by the research workers of Vila Sao José do Murialdo in Brazil. The SRQ questions were read to the patient by one of the three workers, and where necessary, one of the local health workers assisted in translating the questions into Crioulo, the 'lingua-franca' of Guiné-Bissau, or into one of the other languages.

Follow-up

All patients regarded as 'potential cases' had to be followed up, as well as 10% of the 'non-potential cases'. This procedure included the shortened version of the Present State Examination (PSE) administered by the research psychiatrist, the Diagnostic Assessment Form (DAF) completed by the research psychiatrist on the basis of the PSE ratings, a Social Unit Rating (SUR), and in a number of cases a Disability Assessment Schedule (DAS).

Potential cases

We decided that all patients scoring above a certain cut-off point for the total score on the 20 non-psychotic items of the SRQ or scoring at least one positive item on the four psychotic items had to be followed up. The cut-off point was selected to yield optimal sensitivity and specificity, resulting in as few false positives and false negatives as possible. Our cut-off point of seven positive scores was selected on the basis of a pilot test, in the manner of the original study (Harding *et al*, 1980). From the total of 251 screened patients 26 scored 7 or more 'non-psychotic' items, and 59 scored at least one positive psychotic item. Of the latter group, 17 responded as well with a SRQ score of 7 or more, giving a total of 68 potential cases to follow-up. Nine of these 68 potential cases were unwilling or unable to participate, which left us with 59 potential cases for follow up: 18 with a SRQ score of 7 or more, and 54 with at least one positive psychotic item (including 13 with also a SRQ-score of 7 or more). From the group with at least one positive psychotic item, 37 patients scored only on the first item. The notion of being harmed by somebody, especially among patients attending a health institution for any kind of disease, can be considered as a 'normal' attitude in this study area. Therefore, a single score in the first psychotic item did not constitute a potential case. This left us with a total of 22 potential cases for follow-up. We added a further 13 (eight with a positive epilepsy score only, and five who were clinically suspected of being mentally ill).

Apart from the above total of 35 'potential cases', 22 patients were followed-up as a 10% sample of all those scoring less than 7 on the SRQ or who lacked any other indication of being a potential case. It should be noted that of these 22 patients six had a positive score on the first psychotic item. The difference from other centres was that we did not consider a single score on the first psychotic item sufficient indication for follow up, and 13 respondents were added on the basis of various other indications of mental illness.

Results

From the 35 'potential cases', 21 were identified as 'definite cases', and from the 10% sample of 22 patients two were definite cases. The minimum estimate of psychiatric morbidity is therefore 12%: 8.4% identified at follow up and 3.6% on the basis of half the frequency of psychiatric disorder found in the 10% sample. Though the majority were neurotic disorders, we found some psychotic morbidity (14.3%) as is shown in Table I.

Of the 23 'definite' cases, none was detected at the health posts, six in health centres, and 17 in one of the three hospitals. Of the 12 'possible' cases, three were detected at the health posts, seven in health centres, and only two in one of the three hospitals. Taking all 35 cases together, this results in a psychiatric morbidity of 'definite' psychiatric disorders in the health posts, health centres, and hospitals of respectively 0%, 5%, and 16% and 9%, 11%, and 18% including the 'possible' cases of psychiatric disorder. In other words, at a higher level of medical service, more psychiatric morbidity is present, but at a lower level, more patients are found who are thought to be according to the PSE-DAF 'possible' cases of psychiatric illness.

Most patients (72.5%) were diagnosed by the health workers as having physical health problems, 7.6% with physical and mental health problems, 6.8% with a mental health problem only and of another 12.4% it was said to have no health problem.

Since both false positive and false negative diagnoses may be made, it is not only the rate of diagnoses which indicates the diagnostic skill of the health worker. From the comparison of the diagnostic rating of the health worker and that of the research worker the diagnostic sensitivity and specificity can be calculated. These were 31% (11:35) and 88% (191:216).

These two percentages indicate that one out of every three patients with a psychiatric disorder (according to the Diagnostic Assessment based on the PSE) is recognised as such by the health worker, and of every 100 non-cases, 12 patients are wrongly diagnosed by the health worker as suffering from psychiatric illness.

Of the patients wrongly diagnosed by the health worker as suffering from psychiatric illness (25), only one had a non-psychotic SRQ score of at least 7, one scored on at least the second, third, or fourth psychotic item, and none scored on the epilepsy item. Of the patients detected by the screening procedure as cases but not caught by the health worker (24), ten had a non-psychotic SRQ score of at least 7, six scored on at least the second, third, or fourth psychotic item, whereas 17 scored on the epilepsy item. Eleven of the 35 patients with a psychiatric disorder were recognised as such by the health worker: five of these had a depressive neurosis; and the other hypochondriasis, anxiety neurosis, psychogenic paranoid psychosis, affective psychosis or alcoholic hallucinosis. None of the patients with hysteria, unspecified psychosis, epilepsy, paranoid personality disorder, or prolonged depressive reaction was detected by the health worker as suffering from psychiatric disorder.

About 65% of the 251 screened patients quoted one reason for attending the health clinic, 22% two, and 12% three or more. Table II shows the number of reasons for attendance in relation to the diagnosis of psychiatric disorder by the health worker and in relation to the detection of psychiatric disorder by the screening procedure.

Table II shows that patients quoting more reasons have a larger chance of suffering from psychiatric disorder. For patients quoting three reasons, this chance is about one in 3.5, compared with one in nine for patients quoting one reason. Health workers diagnose twice as many psychiatric disorders when patients present two or more reasons for attendance, whereas the screening procedure detects more psychiatric disorders among patients presenting three or more reasons only.

In Table III, all reasons for attendance quoted by at least 5% of the patients are listed. Abdominal pain, chest pain, headache, and pain in arm or leg were each quoted by more than 10%. None quoted any psychological symptom, such as anxiety, confusion, depression, loss of interest, or sleep disturbance.

One of our criteria for selecting the study area was its history during the fighting. We did not find any significant difference in the percentage of psychiatric disorder between those who had remained under Portuguese rule in 'aldeamentos' or 'protected villages'. Further comparison of groups with and without psychiatric disorder did not reveal any socio-economic or cultural characteristics which might be related to such disorder.

TABLE II

Relationship between the number of reasons, the diagnosis of mental disorder by health staff, and the detection of psychiatric disorder by two-stage screening including a psychiatric interview

Number of reasons for attendance quoted by attenders		Cases (%) of psychiatric disorder diagnosed by: (a) Health worker	(b) Two stage screening procedure
1	($n = 164$)	11.6	11.6
2	($n = 55$)	20.0	14.5
3 or more	($n = 29$)	20.7	27.6
Total	($n = 251$)	14.3	13.9

TABLE III

Nine commonest reasons for attendence ranked in order or frequency as rated to diagnosis or psychiatric disorder by health staff and detection of psychiatric disorder by screening procedure.

Reasons for attendance	*Number of patients quoting reasons ($n = 251$)*	*Patients (%), quoting reason, diagnosed by health staff as suffering from mental disorder*	*Patients (%), quoting reason, detected by screening procedure as having psychiatric disorder*
Abdominal pain	55	19.4	17.1
Chest pain	48	8.3	17.1
Headache	36	22.2	28.6
Pain in arm/leg	36	11.1	5.7
Weakness	24	16.7	11.4
General body pain	23	19.4	22.9
Backpain	22	13.9	8.6
Eye problems	17	8.3	2.9
Pregnancy, post natal care	17	5.6	5.7

Discussion

Our conservative estimates show that psychiatric disorders have a morbidity of 12% of those seen in primary health care in our study area in Guiné-Bissau. The recorded frequency falls within the range of 10.6% to 17.7%, found in other developing countries (Harding *et al*, 1980). Disorders detected were mainly neuroses (62.9%), as in other studies (Harding *et al*, 1980; Shepherd *et al*, 1966; Ndetei & Muhangi, 1979), but we did find more psychoses than in other countries. This may be explained by the virtual absence in this case of mental health care. Furthermore, as almost no knowledge of these disorders exists among health workers, psychoses are rarely recognised or referred to the mental health services in the capital. This may be an important reason why these patients can still be found in primary health care in the south of Guiné-Bissau. In addition, a high level of tolerance exists there, causing patients to stay untreated in their villages. The government's purpose is to ensure that primary health workers will play the role of the main agents delivering simple mental health care. Primary health workers live close to the patient, and have contact with the community, hence making them the most suitable people to provide a minimum of mental care at the primary care level at the lowest cost.

However, health workers have to be trained to accomplish this task; at the moment, they recognise only one out of every three patients with a psychiatric disorder, and of every 100 non-cases, they wrongly diagnose 12 patients as suffering from psychiatric illness. It might be that these cases were missed by the research procedure and correctly diagnosed by the health worker, but whichever interpretation is correct, the tendency to miss cases is more important than any risk of over-inclusive diagnosis. It is clear that three priorities can be set for training health workers: psychoses, epilepsy, and neuroses. The first two types of disorders are hardly recognised, whereas the last, which is recognised more often, is a priority because of its much higher frequency. The health worker has to be aware that certain complaints can be a clue to the detection of psychiatric disorder, while any intuitive feeling that 'something is wrong' or that the patient withholds something has to trigger further investigation. This implies that the health worker, apart from excluding physical pathology as much as possible, must look for psychosocial factors and psychiatric symptoms to detect psychiatric disorder. This applies in particular to workers in health centres and hospitals, because cases were particularly missed in these facilities, whereas at health posts, too many patients are diagnosed as suffering from a psychiatric problem.

The next step is to formulate a treatment policy in close collaboration with the family and key persons in the villages. This may include involvement of a traditional healer, solving socio-economic troubles, and other activities to prevent frequent medical attendance, over-consumption of drugs, and a medicalisation of underlying psychosocial problems. This could prevent maladaptive coping mechanisms from getting established during the early stages of the illness, and thereby shorten neurotic conditions particularly.

Our main conclusion is that with additional training, it will be possible to improve health workers' diagnostic skills in recognising patients with neurotic, psychotic, and epileptic complaints. With a limited supply of drugs, together with community participation, referral, and supervision, mental health care will be extended into primary health care in 1984 in the four southern sectors of the study area and will then gradually spread over the other regions.

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Joop T. V. M. de Jong, *Psychiatrist, Head of Department of Mental Health, Ministry of Health and Social Affairs, Bissau, Africa.*

Guus A. J. de Klein, *Sociologist.*

*Sineke G. H. M. M. ten Horn, *Sociologist, Department of Social Psychiatry, WHO Collaborative Centre, Oostersingel 59, Postbox 30.001, 9700 RB Groningen, Netherlands.*

*Correspondence

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Outcome of Patients Committed to Hospital under the Mental Health (Scotland) Act 1960

A. A. MCKECHNIE, A. CORSER and V. R. MCMILLAN

All patients formally detained in a Scottish psychiatric hospital between 1974 and 1979 were identified and their outcome determined 2½–8½ years later. A matched group, detained under Emergency Orders only, were also followed-up. Those formally detained had more previous psychiatric contact: functional psychoses were significantly more common in them. They remained in hospital longer, and required extensive community support when discharged. Those detained under Emergency Orders only, consisted of two sub-groups—one who left the area within two years of admission and could not be traced, and the remainder, who continued to require hospital treatment but for shorter times and with less continuous support. Amongst those detained, lack of insight was a predominant feature, which may create difficulty with regard to informed consent to treatment, given the present Amendments to the Mental Health Acts.

The majority of patients who are admitted to psychiatric hospitals in the UK do so voluntarily, but for a small proportion, compulsory powers are necessary. Because England and Wales, Scotland, and Northern Ireland each have their own legal systems, different Acts are required to comply with the system in each 'Law District'.

To safeguard the rights of patients who did require compulsory powers to be used, the Mental Health Acts of 1959 and 1960 were passed for England and Wales and Scotland respectively. These required two doctors to see and examine any patient, and the application had to be made by the nearest relative or from a Mental Health Officer. In England, there was a section for observation and, if necessary, compulsory treatment for longer periods, subject to review with a right of appeal to the Mental Health Tribunal. In Scotland, an application had to be submitted to a Sheriff, who could hear objections from the patient or relatives; appeals against detention were also made to the Mental Welfare Commission, or to the Sheriff when the order was reviewed. An Emergency Order was available in England for 72 hours, which required one doctor only to see and examine the patient; the consent of a relative or Mental Welfare Officer was usually obtained. In Scotland, this was in pursuance of full detention under Section 24 and was for seven days. The main differences were the ability to detain patients for observation in England and the more elaborate appeal procedure in Scotland.

Both countries empowered the police to admit "as to a place of safety" mentally disordered people found in a public place and in need of immediate care and control. Such a patient could be detained longer than 72 hours and during this time, he had to be examined and a decision made with regard to his need for in-patient treatment. A very small proportion of patients were also detained in psychiatric hospitals when Criminal Courts made a hospital order rather than impose a prison sentence. The Acts allowed people to be detained for a limited period of time for observation as well as for treatment. Some patients require conditions of maximum security, and there are State or Special Hospitals which provide this facility to which patients may also be transferred there when already detained under the above Sections of the Acts.

In both countries, Amendments to the Act will have important implications (see Appendix); these now allow short-term detention in Scotland (Section 26 (1984)) for 28 days, and have introduced a Mental Health Act Commission in England and Wales. The Amendments also include specific changes in consent for treatment, more regular reviews of detained patients, and more responsibility by the Local Authority Social Work Department for detained patients.

Despite the time these Acts were in force and the more recent Amendments, actual studies relating to compulsory detention and the outcome of such hospital admissions remain few. In Scotland, both Elliott *et al* (1979) and Chiswick (1980) identified an apparent anomaly in the increased number of

Emergency detentions (Section 31/32, i.e., people detained for seven days), sometimes repeated two or three times consecutively, without the Full Recommendation (Section 24) being pursued. In England, there was a substantial rise in the Place of Safety Order, Section 136; in Scotland, the equivalent, Section 104, is used infrequently, except in Aberdeen (Scottish Statistics).

Elliott *et al* (1979) reported that 10.5% of all admissions in Scotland were compulsory, and a similar pattern was apparent with admissions to Bangour Village Hospital, West Lothian District. In the latter, the majority were Emergency Seven-Day Orders (Section 31/32), less than one-third of which went to full section. Very few patients were admitted directly from the community under Section 24 (Full Recommendation), most being detained first under Section 31. A small number, about one each year, were detained from the Courts following criminal proceedings.

No longitudinal studies have been published describing the outcome of detained patients in Scotland. In England, Szmukler *et al* (1981) has made a comparison between informal and formal patients with a report on outcome one year after detention. For these reasons, and despite the limitations of a retrospective study, a follow-up study was undertaken of patients detained within Bangour Village Hospital.

Aims of the Study

1. To identify some characteristics of patients aged 16–64 fully committed to a Scottish psychiatric hospital.
2. To compare these characteristics with a matched group of patients who had been detained using emergency powers only (Section 31/32) of the Mental Health (Scotland) Act 1960.
3. To consider differences between these two groups with regard to: (a) previous psychiatric contact (b) diagnosis and duration of in-patient stay following admission (c) outcome after discharge from hospital

Method

The psychiatric services for West Lothian, including the New Town of Livingston, were the main source of subjects. The population, initially 123,000, had risen to 140,000 by 1980; most people live in small towns of 5–15,000. Seventy-seven percent of houses are publicly owned (Council tenants), with a preponderance of lower socio-economic groups and relatively high unemployment. All patients, male and female aged 16–64, who were detained in hospital between 1974 and 1979 were identified through the Medical Records Department's Register of Compulsory Patients.

Two groups were identified. The first included those where a Full Recommendation (Section 24) had been made and all those detained as a result of a Court Order following criminal proceedings. The second group was matched, as far as possible, for age (within three years), sex, and time of admission. This group had been detained using the Emergency Order only, without pursuance of full compulsory powers, because the acute crisis passed and people were willing to stay in hospital if further in-patient treatment was advised.

A coding sheet was prepared which identified age, sex, details about previous history, diagnosis and outcome. In particular, information was sought about duration of stay, type of follow-up, and utilisation of support services. Where patients had been discharged, their current general practitioners were contacted and a simple questionnaire sent; this information was sometimes obtained from the Primary Care Division of the Lothian Health Board. Patients who had care continued in other psychiatric hospitals were contacted and up-to-date information obtained. A census date was taken as at 31 July 1982. Patients who had died or remained continuously in hospital were considered in relation to variables affecting admission. The total follow-up varied between 2½ and 8½ years, depending upon year of admission for the survivors.

Further information was obtained from patients who had been admitted under Full Recommendation from either the legal documents or the clinical notes. The information included suicidal threats or parasuicide, statements about violent behaviour, whether the individual had insight, etc. All information was coded and processed using the facilities of the Edinburgh Regional Computer Centre (University of Edinburgh). Once coded, information was tabulated and analysed.

Results

A total of 111 formally detained patients were identified with a further four excluded because of inadequate information. The average number was just over 18 per annum, with a range of 5–26 in each year. There were 57 matched controls, detained under Emergency Orders (Section 31/32); 50% of those Fully Recommended (R Group) were already in hospital and only 30% were detained from the community. Emergency Orders (E Group) were applied in the matched sample in 35% (Section 32) of the cases in hospital; 44% were from the community and 21% (Section 31) from the District General Hospital. Eight people were admitted following criminal proceedings, four directly from Court and four transferred from the State Hospital.

Socio-demographic data

Of the R Group, 58% were men; the average age was 37 years, with 61% below the age of 44. In the matched E Group, 54% were men, the average age being 33, with 70% below the age of 44. Of the R Group, 44% were single, compared with 28% of the matched sample. Unemployment was high in both groups—54% and 42% respectively. More of the R Group were living with their parents. Amongst those fully detained, 62 had been married and of these, 39% were divorced, separated, or widowed, compared with 17% of the E Group ($n = 41$).

Previous psychiatric contact

The number of out-patient contacts, hospital admissions, and the total length of time as an in-patient was determined over a four-year period before the key admission. Three-quarters (75%) of the R Group had had previous psychiatric contact, compared with 47% of the E Group; this was statistically significant ($x^2 = 12.51 < .001$ with 1df). The pattern of previous admissions and the duration of time in hospital in weeks showed marked differences, with more frequent and longer time in hospital being more common in the fully detained category.

Diagnosis and reason for recommendations

Table I shows that amongst those fully committed, half (50%) had a diagnosis of schizophrenia, whereas 19% of the E Group were in this category. There were 10% with affective psychosis in the R Group and 18% in the other. There was a significant excess of functional psychosis in the R Group, but 12% of those fully detained had alcoholism as their principal diagnosis.

The reasons given on the recommended form for being detained were examined, but no attempt was made to classify actual psychotic symptoms or behaviour. The most common reason recorded was unwillingness or inability to co-operate in treatment either as in- or out-patient; 44% were in hospital for the protection of others, although violent behaviour was recorded in a slightly higher number. Threats of violence were more frequent than actual injury to family members or others. Suicidal risk was judged to be apparent in 39%. Disturbed behaviour, inability to care for one-self, and lack of insight were found in over half.

TABLE II

Outcome of fully detained and emergency section patients (July 1982)

	Fully detained *n = 111*	*Emergency section* *n = 57*
	%	%
Discharged, no further admission recorded	24	14
1 further admission	11	12
2 or more admissions	35	33
(Further admissions under Section)	30	14
(Continuous in-patient care (including transfer)	18	—
Discharged, left district within 2 years and untraced	2	35
Died	10	6

Outcome

Table II shows the outcome by July 1982. All but two of the R Group were traced, and 24% had had no further admissions; 18% were in continuous care, including five transferred to other hospitals (three in the State Hospital), and 46% had required readmission. But 45% in the E Group also required readmission, and this may be an underrepresentation, in that a full follow-up throughout this period was not obtained for 20 people. Amongst those detained, 11 had died, including three suicides, whilst three had died in the matched sample. Excluding the deaths and those who had remained continuously in hospital, there were 78 in the R Group and 54 in the other. Further detention orders were required in 30% of the former cases, but in only 14% of the latter.

Those who had been fully committed spent considerably more time in hospital: 28% were out of hospital within 14 weeks, 27% were in between 15 and 49 weeks, and 45% in for more than one year. By comparison, 65% of the E Group were discharged within four weeks and a very small number were in-patients for more than 15 weeks.

The type of follow-up given to those discharged was different, in that more of the R Group were attending day hospitals and lithium and depot phenothiazine clinics. The proportion receiving out-patient follow-up and home visits were similar in both samples, but the duration of follow-up was markedly different between the two, with more recommended patients followed up for much longer. In fact, just 30% were completely discharged from the R

TABLE I

Final or discharge diagnosis

		Fully detained *n = 111*		*Emergency section* *n = 57*	
Psychoses *(ICD 280–299)*	Schizophrenia and paranoid states	54 (49%)		11 (19%)	
	Affective psychosis	11 (10%)	68%	10 (18%)	44%
	Other psychosis	10 (9%)		4 (7%)	
Neurosis & Personality Disorders *(ICD 330–309)*	Alcoholism	13 (12%)		13 (23%)	
	Poisoning by drugs		32%		56%
	Neurotic disorders, personality disorders	23 (20%)		19 (33%)	

$x^2 = 8.79$ $P > .01$ 1df

Group, while a third had contact for up to three years, and the remainder for more than three years. In the matched sample the pattern was quite different, with much shorter follow-up contact recorded; although they did receive considerable support, it was generally required for shorter periods of time.

Discussion

Compulsory powers to admit patients for treatment are used in about 10% of all admissions, and in Scotland, most orders are Emergency Orders, which are not pursued to full committal. In this study, two separate groups were identified over a six-year period, viz—all of those fully committed, and a smaller group, matched for age, sex, and approximate time of admission, who were detained on an Emergency Order only. Generally, this picture complies with the findings in other Scottish Surveys (Masterton *et al*, 1982; Chiswick 1980) and is in marked contrast to the London findings of Szmukler *et al* (1981), where the bulk of emergency referrals were by the police, using Section 136.

In just under a third of those fully committed, the procedure commenced at home, but a higher proportion of the Emergency Group only originated from home. Most of those fully committed were subject to an Emergency Order; in both groups, more orders were instigated in a hospital setting rather than at home.

Almost half of those fully committed were single, and in contrast with the matched group, they were more likely to be single, or if they had been married, to be separated or divorced. Most of those detained, particularly in the matched group, were not living with parents. Unemployment was high in both groups; generally, these findings are in keeping with those of Elliott *et al* (1979). Nearly 70% were below the age of 45, which is similar to the findings of Bean (1980), although in his study more women required compulsory detention. Szmukler *et al* (1981) had found a higher proportion of single subjects, who were more likely to be living alone or in lodgings, and with an even higher unemployment rate. In the West Lothian population, extensive contact remained with families, and a substantial group was still living with parents.

More of those in the detained group had previous psychiatric contact, many having had several admissions in previous years. Generally, functional psychoses were more prevalent, although overall, neuroses and personality disorders were more common than in other Scottish studies (Elliott *et al*, 1979).

Those who require detention are a very disabled group. In a national survey of 'New' long stay patients (Mann & Cree, 1976), 50% of those who required long-term care as in-patients, or further in-patient treatment before they were likely to be discharged, were formally detained in hospital. Furthermore, disturbed behaviour occurred when medication was discontinued, supervision seemed to be essential, and "patients on treatment orders appeared more disturbed, many requiring skilled nursing care and close supervision". This is amply borne out in the present study, and even when discharged, this group required extensive community support; they required longer spells of in-patient care and substantially more community support through day hospital, depot-phenothiazine clinic, and lithium clinic attendance. Mortality also appears high in such a young age-group—10%, including three who had committed suicide.

The outcome was known in 95% of those fully detained. The matched Emergency Group could be sub-divided into two: one group had left the district within two years, and could not be traced; the second continued to present for psychiatric treatment, including further in-patient care, but did not require such extensive community support, needed shorter further in-patient periods, and fewer further compulsory orders.

The Mental Health (Scotland) Act stated that a full order can only be pursued where, given evidence of illness, the person's health or safety is at risk, or for the protection of others; and required a statement detailing why other forms of care, including informal admission, were *not* possible. Masterton *et al* (1982) concluded that a seven-day detention order would appear more relevant, and this is borne out by this study. This is now superceded in the new Scottish Act by a short-term (28 days) detention order, but retaining the right to appeal to a Sheriff. Over 50% of those detained under an Emergency Order only had no previous psychiatric contact, and their admission usually followed an episode of self-injury or self-poisoning. These findings tend to support Chiswick's (1980) contention that this is "compulsory crisis intervention", not requiring longer-term treatment regimes. But as a group, excluding those who left the area, they do continue to require psychiatric contact, which in most instances they subsequently seek on an informal basis.

Amongst those fully detained, the major reason given for this order was unwillingness or inability to co-operate with treatment, and 54% lacked insight. Violent behaviour was present in 52% and 44% were judged to require detention for the protection of others. Actual injury to family members was seen in less than 10% altogether and most of these came within the small number detained through a Criminal Court Order. The Act in Scotland spells out "in the interest of the patient's health or safety"—*not* just danger. Lack of insight was recorded in just over half of those formally detained. This was also a feature in Szmukler's study, and he commented that "only about half of the informal patients felt they were psychiatrically ill and needed to be in hospital, (this) is noteworthy". Lack of insight is commonly found in severe functional psychoses and does create considerable difficulties in relation to requirements for informed consent to treatment.

The Amendments to the Acts reduce the length of time for emergency detention in Scotland, but introduce a short-term order of up to 28 days. There is an increase in the contribution from Social Workers, despite the evidence that Local Authority services for the mentally ill, especially after care, are grossly inadequate in Scotland, receive a low priority, and are currently threatened with further reduction. The main change is in relation to consent for treatment; given the findings in the survey and that of Szmukler *et al*, this is going to increase workload substantially. Thus the rights of severely disturbed people to receive care and treatment may be further diminished, if medico-legal caution overrules clinical judgment.

The best safeguard to patients' welfare must remain a properly funded and staffed comprehensive psychiatric service, with properly conducted long-term prospective studies of the outcome of patients requiring detention. Because different laws operate within the UK, compulsory admissions will vary considerably, but even within these 'law' districts, there is also some evidence of inter-regional differences in the use of compulsory powers.

Unfortunately, nationally derived data refer to episodes of illness and do not assist in charting outcome over lengthy periods of time. The case register affords the opportunity for studies based on cohorts, and several such exist within the UK. It is vital that proper prospective studies are undertaken now, given the Amendments to Acts relating to compulsory admission. These studies need to be instigated straight away.

Acknowledgements

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Appendix

Principal corresponding sections of the relevant Mental Health Acts for England & Wales and Scotland

	England & Wales		Scotland	
	1959	1983	1960	1984
Admission for assessment	25	2	—	26
Admission for treatment	26	3	24	18
Emergency admission	29	4	31	24
Emergency detention of informal patient	30	5	32	25(1)
Nurses holding power	—	5(4)	—	25(2)
Place of Safety Order (Persons in Public Places)	136	136	104	118
Mentally abnormal offenders	1959	1983	1960	1975*
Hospital order	60	37	55	175/376
Restriction order	65	41	60	178/379

*Criminal Procedure (Scotland) Act (1975)—replaced Part V

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*A. A. McKechnie, MD, FRCPsych, *Consultant Psychiatrist, Bangour Village Hospital, Broxburn, West Lothian.*

Alison Corser, BSc Hons, *Post-Graduate Student, Edinburgh University.*

Mrs V. McMillan, *Medical Records Officer, Bangor Village Hospital.*

*Correspondence

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Adverse Drug Reactions to First- and Second-Generation Antidepressants: A Critical Evaluation of Drug Surveillance Data*

L. G. SCHMIDT, R. GROHMANN, B. MÜLLER-OERLINGHAUSEN, H. OCHSENFAHRT and P. S. SCHÖNHÖFER

We reviewed data on adverse drug reactions (ADRs) to first- and second-generation antidepressants, recorded by two different drug surveillance systems. The rate of ADRs that led to discontinuation of the drug in the individual case, assessed within a multi-centred hospital-based drug monitoring system (AMÜP), was significantly higher in case of exposure to tricyclics (7.4%) than with the second-generation drugs (3.1%). On the basis of voluntary reports to the Medicines Commission of the German Medical Profession (AMK), profiles of ADRs to the drugs under survey were constructed and compared with data compiled by the WHO. The types of ADRs varied more between second-generation drugs than between tricyclics. Special attention was paid to rare but serious ADRs (e.g. seizures during treatment with maprotiline, and blood dyscrasias attributed to mianserin).

The clinical efficacy of first- and second-generation antidepressant drugs has been proven by a large number of controlled clinical trials. However, the evaluation of drug safety has lagged behind; partly because, for ethical reasons, treatment conditions cannot be varied systematically for analysis of adverse drug reactions (ADRs). Systems for surveillance of drugs already on the market have been established in recent years in order to provide information on drug risks in large populations. In order to assess possible differences between the quality and frequency of adverse reactions to first- and second-generation antidepressants, we analysed data available in two drug surveillance systems operating in West Germany. In this survey, the first generation of antidepressant drugs is represented by amitriptyline, clomipramine, dibenzepin, and doxepin, whereas the second generation is represented by nomifensine, mianserin and zimelidine. Maprotiline is viewed as an 'intermediate' compound.

Method

1. Drug surveillance in hospitals (AMÜP)

A drug surveillance system has been established by AMÜP (*Arzneimittelüberwachung in der Psychiatrie*) in several psychiatric hospitals in West Germany since 1979 in order to investigate ADRs due to psychotropic agents (Rüther *et al*, 1980; Grohmann *et al*, 1984; Schmidt *et al*, 1984). An ADR is defined as a noxious and unintended response in man to a drug administered at a dose appropriate for prophylaxis, diagnosis, or therapy (Karch & Lasagna, 1975). Monitoring of ADRs in the AMÜP system is performed by specially trained psychiatrists who contact the ward physicians of collaborating hospitals at weekly intervals. All necessary information is obtained from the treating physicians by a structured interview and is registered on special forms for computer-evaluation. ADRs are classified on the basis of the AMDP system (Arbeitsgemeinschaft für Methodik und Dokumentation in der Psychiatrie, 1981). The *causal relation* between the occurrence of an ADR and the administration of a drug is assigned one of three grades of probability: *possible*, *probable*, or *definite* (Seidl *et al*, 1965; Hurwitz & Wade, 1969). The assessment of ADRs is performed by case-conferences, each headed by an experienced clinical psychopharmacologist. Only cases that were assessed as 'probable' or 'definite' were included in the present study. Regarding *severity*, an ADR is assessed in our system according to its impact on the treatment of the patient: only ADRs that had led to the discontinuation of the medication blamed for the ADR were taken into account for this report.

All drug exposures recorded in the psychiatric hospitals of the Berlin and Munich universities from 1979 to 1982 were used for calculating the frequencies of various types of ADR. An exposure was defined as the administration of the drug irrespective of dosage and duration of use. Methods for assessing drug utilization and patterns of prescribing drugs in the Berlin and Munich hospital have been published earlier (Grohmann *et al*, 1980; Schmidt *et al*, 1983); and the methodology of assessing ADRs and some epidemiological findings are described in detail elsewhere (Grohmann *et al*, 1984; Schmidt *et al*, 1984).

2. Voluntary reporting by physicians (AMK)

A voluntary reporting system is run by the Medicines Commission of the German Medical Profession in

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**Dedicated to Professor H. Hippius, Head, Dept of Psychiatry, University of Munich, on the occasion of his 60th birthday.*

Cologne (*Arzneimittelkommission der deutschen Ärzteschaft* = AMK). Data included in AMK are based on voluntary reports from physicians practising in either private practice or hospitals all over West Germany. For this evaluation, all ADRs listed in the reports by March 1984 were coded using the WHO terms based on classes of organs or physiological functions. For constructing 'ADR profiles' the number of ADRs in each class was calculated as a proportion of all the ADRs reported for each compound. Data on drug exposures could not be taken into account in this analysis.

3. WHO collaborative centre

Information on selected ADRs was obtained from the WHO collaboration centre in Uppsala (Sweden) and arranged in profiles as described above. Categories of ADRs are presented here only as proportions of all ADRs to a certain drug because of confidentiality of filed WHO data.

TABLE I

Drug exposures and adverse reactions (ADRs) to first- and second-generation antidepressants in AMÜP-hospitals, 1979–1982.

Drug	Number of exposures	Number of ADRs	ADRs per 100 exposures
First-generation			
amitriptyline	1369	97	7.1%
clomipramine	513	53	10.3%
dibenzepin	407	42	10.3%
doxepin	377	5	1.3%
Total	2666	197	7.4%
"Intermediate":			
maprotiline	426	39	9.1%
Second-generation:			
mianserin	335	10	3.0%
nomifensine	180	6	3.3%
zimelidine	0	0	0
Total	515	16	3.1%

Results

1. The hospital study

Recorded exposures to the surveyed antidepressants from 1979 to 1982 in the Berlin and Munich hospitals numbered 3607. The relation of ADRs to number of exposures is listed in Table I: the discontinuation-rates ranged from 1.3% for doxepin to 10.3% for clomipramine and dibenzepin. ADRs occurred less frequently with the second-generation drugs (3.1%) than with the tricyclics (7.4%), and the difference was statistically significant ($\chi^2 = 10.4$, d.f. = 1, $P < 0.001$). ADRs to maprotiline were also significantly more frequent than to the second-generation drugs ($P < 0.001$).

The frequencies of different ADRs as well as the mean age and sex of patients who had developed ADRs to each drug are listed in Table II. Patients with ADRs to

TABLE II

Frequencies of ADRs to first-generation antidepressants, maprotiline and second-generation antidepressants. The values in the table represent the number of patients with ADRs as a percentage of patients exposed (AMÜP in-patients, 1979–1982)

	First generation					Second generation	
	amitriptyline	clomipramine	dibenzepin	doxepin	maprotiline	mianserin	nomifensine
Patients with ADRs	*n* = 97	*n* = 53	*n* = 42	*n* = 5	*n* = 39	*n* = 10	*n* = 6
Sex	68%F:32%M	82%F:18%M	79%F:21%M	100%F:0%M	82%F:18%M	80%F:20%M	84%F:16%M
Mean age (years)	53.9±	49.6±15.9	62.0±16.1	54.0±21.6	55.7±15.8	61.0±16.4	56.3±17.6
Adverse reactions:							
Toxic delirium	1.53	0.77	2.21	0.26	1.41	0.29	0.55
Confusion	1.31	0.58	2.45	0.26	0.70	0.59	0.55
Delusions	0.80	0.97	1.22	—	1.16	0.29	—
Psychomotor disturbance	1.16	1.55	2.94	0.26	0.70	0.29	0.55
Oversedation	0.58	0.58	—	0.53	0.23	—	—
Inability to concentrate	0.58	0.58	1.71	—	0.46	0.59	—
Mood disturbance	0.80	2.33	1.22	—	0.93	0.29	—
Increased drive	0.14	1.94	0.98	0.26	0.46	—	0.55
Sleep disturbance	0.21	1.55	1.22	0.26	0.46	0.29	0.55
Dizziness	0.43	0.97	0.73	—	1.39	0.29	—
Urinary retention	0.87	0.58	0.73	—	0.23	—	—
Sweating	0.65	1.36	1.47	0.26	0.23	—	—
Increased transaminases	0.65	0.97	1.96	—	0.93	0.59	2.22
Exanthema	0.29	0.19	1.47	—	1.16	0.29	—
Fever	0.07	0.19	—	—	—	—	2.22

dibenzepin and mianserin were the oldest, patients with ADRs to clomipramine were the youngest, but there were no statistically significant differences between the average ages of the groups.

Toxic delirium, drug-related confusion and delusions were prominent ADRs of the tricyclics and of maprotiline. Psychomotor disturbances, mostly agitation or inner restlessness, were typical adverse reactions to tricyclic drugs, especially dibenzepin, but not to the second-generation antidepressants. Mood disturbances, increased drive and sleep disturbances occurred most frequently with clomipramine. Sweating and urinary retention were common for the first- but not for the second-generation drugs. Dizziness was a relatively frequent factor in ADRs in patients treated with tricyclics, maprotiline and mianserin. Impaired liver-function tests and fever reactions were observed most frequently in patients treated with nomifensine.

Analysis of rare but severe ADRs revealed that convulsions occurred in two of the 426 patients treated with maprotiline. Both patients were on lithium and one additionally on perazine: both had a history of head injury. Two further cases of convulsions were observed among the 1369 amitriptyline-treated patients; both patients were also on either perazine or biperiden. Regarding blood dycrasias, there was one case of reversible granulocytosis during treatment with maprotiline and perazine.

2. Voluntary physicians' reports

ADR profiles based on voluntary reports by physicians to the AMK are shown in Figure 1: 265 ADRs were reported for first-generation antidepressants, 141 for second-generation antidepressants, and 115 for maprotiline. The profiles of the tricyclics are all similar: the most common reactions were CNS effects (anxiety, hallucinations, tremor, convulsions); autonomic effects (urinary retention, blurred vision, sweating, dry mouth); and cardiac reactions (tachycardia, conduction disturbances, arrhythmias). In contrast, each second generation drug (and, maprotiline) had a unique profile, with peaks at CNS and skin reactions (exanthema, pruritus) for maprotiline; at CNS and liver reactions (increased transaminases, jaundice) for mianserin; at fever and liver reactions for nomifensine; and at CNS and gastrointestinal reactions (nausea, vomiting) for zimelidine.

Certain serious ADRs appear to be associated with certain drugs. Convulsions had been reported in 12 of the 46 CNS reactions due to maprotiline: these 12 reports accounted for 63% of all convulsions reported for the first- and second-generation drugs, even though reports related to maprotiline accounted for only 22% of the reports on all eight drugs. Similarly, nomifensine was responsible for 39 reports of fever and 17 reports indicating hepatotoxic effects; and in five cases it was blamed for inducing immunohaemolytic anaemia, with non-fatal renal failure as sequelae in two cases. (*See also* Postscript) Because of the small number of reports related to mianserin and zimelidine, analysis of single ADRs appears to be of limited validity.

3. Data from the WHO

Data on selected ADRs of the second-generation drugs, of maprotiline, and of amitriptyline as a reference drug, were obtained from the WHO collaboration centre (Figure 1). There is clear evidence of a disproportionate number of convulsions due to maprotiline, while mianserin is notable for causing blood dyscrasias and sleep disturbances: by October 1983 about 60 cases had been reported, from several countries, which involved mianserin in blood dyscrasias (leucopenia, agranulocytosis, aplastic anaemia). In most cases the syndromes occurred during the 4th–6th week of treatment, and mostly at standard doses of 30–60mg/day, indicating a myelotoxic reaction. Some cases of aplastic anaemia had a fatal outcome. Mianserin was also reported to cause a typical syndrome of painful swelling of small joints, with or without impaired mobility.

The WHO data also confirm the excessive number of fever and liver reactions to nomifensine and zimelidine. Zimelidine is also known to cause hypersensitivity reactions that are sometimes followed by disturbances of the central and peripheral nervous sytems: according to Nilson (1983), there had been eight cases of Guillain-Barré syndrome, four cases of facial paresis and nineteen neuropathies recorded in Sweden by September 1983, when the drug was withdrawn from all countries by the manufacturers because of the ADRs. Our analysis of such cases revealed that in certain patients the symptoms persisted for as long as four years after the drug was discontinued.

Discussion

The aim of this investigation was to give a detailed survey of drug surveillance data on selected antidepressants currently available in West Germany (including zimelidine, which has now been withdrawn). Special attention was paid to adverse drug reactions that are of clinical relevance for the treating physician: we therefore used drug discontinuation as the major criterion for recording an adverse drug reaction in the AMÜP system. The data from the Medicines Commission (AMK) and the WHO were also based on drug discontinuation in the majority of cases.

In that the type of ADR recorded depends on the type of drug surveillance system used, each approach to recording ADRs has its strengths and weaknesses. The data collected by the AMÜP were systematically obtained from in-patients of two university psychiatric hospitals by specially-trained drug monitors. Being a hospital-based drug monitoring system, the AMÜP can provide detailed information on common ADRs, especially with respect to their frequencies. The findings from the AMÜP also showed that drug discontinuation occurred less frequently with second generation antidepressants than with tricyclics. It should be

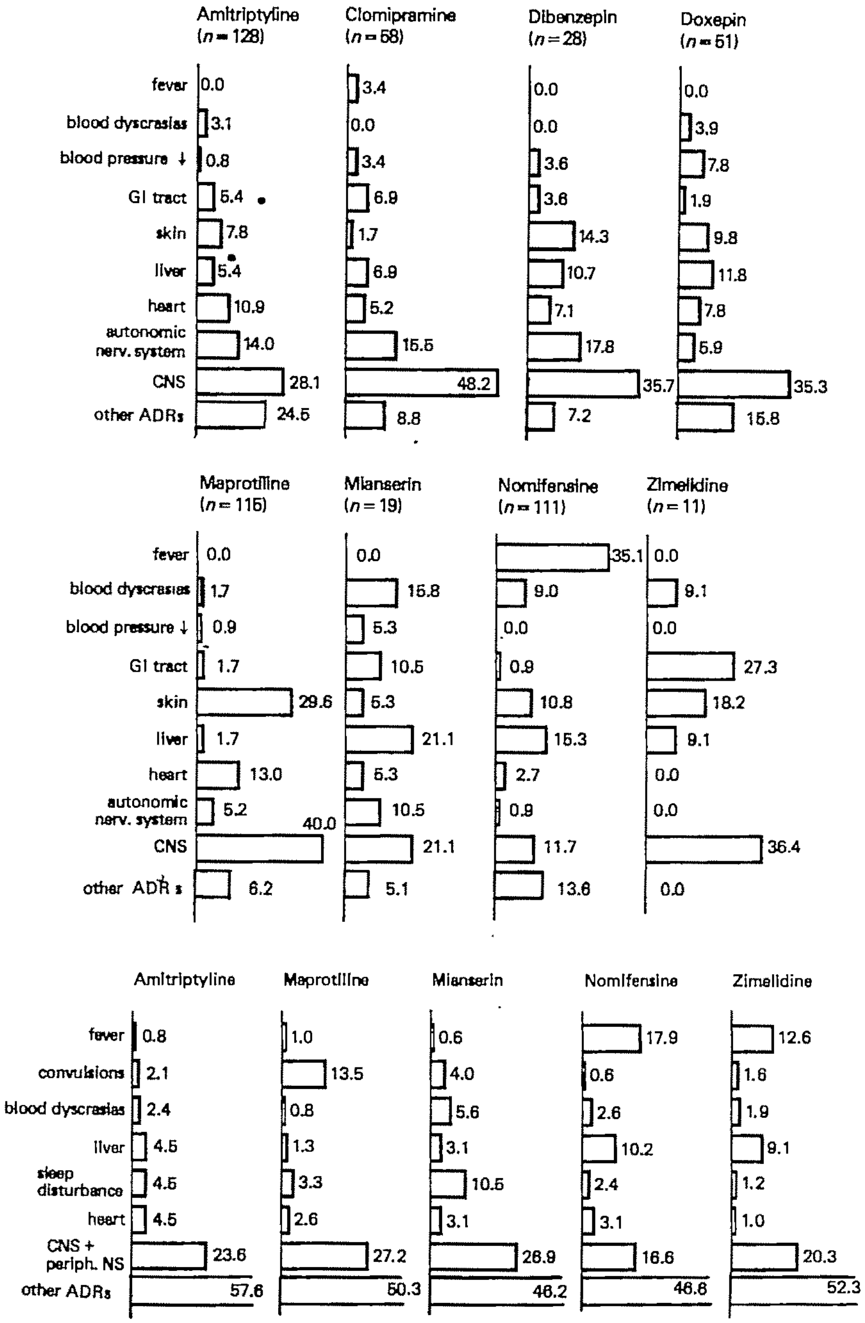

FIG. 1. ADR profiles: each bar represents the percentage of adverse drug reactions to that particular drug which fall into that category (CNS/heart/liver, etc.—categories based on WHO classification).
Top row: First-generation antidepressants (data collected by the Medicines Commission—AMK—on the basis of voluntary reports by physicians)
Middle row: Maprotiline and second-generation antidepressants (data collected by AMK on the basis of voluntary reports by physicians)
Bottom row: WHO date for comparison

noted, however, that phase IV-studies are not based on randomization of patients, so that differences between ADR rates in the AMÜP may also reflect differences regarding indications, drug dosages or patient variables. For example, doxepin's moderate rate of ADRs may be attributed partially to its use in low dosage for treating withdrawal syndromes in drug addicts and drug abusers, while the higher rate of ADRs for dibenzepin may correspond to its frequent use for elderly patients.

The data obtained by the AMK were based on voluntary reports by practising physicians (e.g. general practitioners, internists, neurologists, and psychiatrists) treating in- and out-patients all over West Germany. Systems for collecting voluntary reports on side-effects of drugs are operating in several countries in order to detect rare but serious ADRs, thus giving warning of risks not usually discovered in clinical trials. Reliable data from such systems can also be used for constructing ADR profiles (Inman, 1980). The data in AMK show that the ADR profiles of tricyclics were all similar, whereas the profiles of the second-generation antidepressants and of maprotiline differed markedly from each other. As to the validity of the AMK data, it should be mentioned that reports of ADRs are generally not received regularly by the collecting centres; the frequency of reports depends on variables such as seasonal influences and a decrease of reporting in the third year after drug approval (Weber, 1984). Drugs which have been on the market for some time (e.g. the tricyclics) have had longer to show their side-effects; but newer drugs may have been subject to more critical scrutiny, as progressively more attention has been paid to drug safety. Such variables may be responsible for the general under-representation of reports on ADRs to tricyclics. Therefore no conclusions can be drawn from these data regarding either the actual incidence of ADRs or chronological trends in ADRs.

The WHO data were obtained for comparison and to provide additional information about some rare ADRs. The occurrence of convulsions in patients receiving maprotiline is controversial (Grüter & Pöldinger, 1982), but our data provide additional evidence that there *is* a special risk of maprotiline inducing seizures in predisposed patients. According to Wells & Gelenberg (1981), and a report of the drug's manufacturer on clinical trials of maprotiline (CIBA-GEIGY, December 1980, unpublished), the frequency of convulsions in clinical trials is estimated at between 0.1 and 0.2% of exposed patients.

As to mianserin, the risk of drug-induced blood dyscrasias became evident after 10 cases had been detected in the course of 50000 drug exposures to mianserin in Australia. In Great Britain, 34 cases of blood dyscrasias were noted in response to 1200000 mianserin prescriptions, but the rate of under-reporting is unknown. Likewise, the syndrome of swelling in small joints induced by mianserin may often be overlooked, especially in elderly patients, among whom the prevalence of osteoarthritis is high.

Current investigations aimed at evaluating rare drug risks are impeded by the very heterogeneous nature of available data (Venulet, 1979). Further attempts to assess rare but severe drug risks and to identify high-risk patients have to be made in the future.

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Postscript

After completion of this manuscript, six reports of severe allergic alveolitis/interstitial pneumonia due to nomifensine treatment were received by AMK.

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*Lutz G. Schmidt, MD, DiplPsych, *Consultant Psychiatrist, Department of Psychiatry of the Free University of Berlin, Eschenallee 3, D-1000 Berlin 19 (West), Germany*

R. Grohmann, MD, *Consultant Psychiatrist, Department of Psychiatry of the University of Munich*

B. Müller-Oerlinghausen, MD, *Professor and Head of the Laboratory of Clinical Psychopharmacology, Department of Psychiatry of the Free University of Berlin*

H. Ochsenfahrt, MD, PrivDoz, *Medicines Commission of the German Medical Profession, Cologne*

P. S. Schönhöfer, MD, *Professor and Head of the Institute of Clinical Pharmacology, Bremen*

*Correspondence

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Mydriatic Response to Topical Naloxone in Opiate Abusers

A. H. GHODSE, T. H. BEWLEY, M. K. KEARNEY and S. E. SMITH

Naloxone hydrochloride eyedrops 1 mg/ml dilated the pupils of 36 out of 47 opiate addicts on methadone maintenance treatment, without precipitation of acute withdrawal effects, but not those of healthy unmedicated subjects. The response in addicts was attenuated by certain ancillary treatments and by withdrawal of methadone treatment. The size of the response suggests some potential clinical use for topical naloxone as a diagnostic test of current opioid influence and possibility of physical dependence. The local mydriatic response, which was restricted to the treated eye, indicates that the effect of opiates on the pupil in man is determined, at least in part, by a peripheral action.

Opiate analgesics and opioid derivatives constrict the pupil in man and it is widely assumed that this effect arises from a central stimulant action, resulting from removal of central inhibition on the Edinger-Westphal nucleus in the mid-brain (Lee & Wang, 1975). It has, however, been reported that high concentrations of morphine applied topically constrict the pupil (Nomof *et al*, 1968) and that topical naloxone produces a mydriatic response in opiate addicts (Fanciullacci *et al*, 1980; Del Bianco *et al*, 1981). Such findings imply that a peripheral action may contribute to the miotic effect of opiates, and raise the interesting possibility that naloxone eyedrops in patients and healthy voluntest of opiate dependence without the attendant risks and discomfort of systemic withdrawal effects. We tested this possibility in a prospective study of naloxene eyedrops in patients and healthy volunteers.

Method

Studies were performed on 20 healthy volunteers (nine F, 11 M) aged 18 to 61 (median = 30) years, and on 47 in-patient opiate addicts aged 22 to 57 (median = 31) years on maintenance methadone treatment 10 to 120 (mean = 43) mg/day, six hours after the morning dose. None of the healthy subjects but seven of the opiate addicts had other drugs prescribed (one patient each: phenytoin, chlorpromazine, fluphenazine + procyclidine, pentobarbitone, trimipramine; two patients: thioridazine). Naloxone eyedrops 1 mg/ml were freshly prepared in isotonic phosphate buffer, pH 6.5, two drops being instilled, one minute apart, into one conjunctival sac. Diameters of both pupils were measured before and at 30, 45, and 60 minutes following drug instillation by infra-red television pupillometry in subdued ambient lighting by methods previously described (Smith *et al*, 1978). Reproducibility of this method has been assessed in this laboratory by repeat measurements of darkness diameter in 20 healthy subjects; the within-subject coefficient of variation was 2.8%.

In 15 of the opiate addicts only, symptoms of opiate withdrawal were sought before and at 60 minutes after eyedrop instillation, using a slight modification of the Self-Report Questionnaire of Narcotic Withdrawal (Martin *et al*, 1973). Urine samples taken from the opiate addicts at the time of the investigation were screened for illicit drugs: one only was positive for diamorphine and codeine.

Twelve of the opiate addicts were re-tested on a second occasion following slow withdrawal and cessation of methadone treatment. In these subjects, the test was applied 2–7 days after the last dose of methadone.

Results

Mean pupil diameters of both eyes in healthy volunteers and the first 20 opiate addicts studied, before and at various times after naloxone instillation, are shown in Figure 1. There was no significant diameter change of either eye in the healthy subjects, but a mydriatic response was observed in the treated eyes only of opiate addicts ($P<0.001$), with a median time to maximum response of 45 minutes. The magnitude of the individual maximum drug effects in all healthy subjects and 47 opiate addicts, calculated as the diameter difference at 45 minutes between the two eyes corrected for any initial anisocoria, is shown in Figure 2. Thirty six (77%) of these values were outside the 'normal' range (mean±2 standard of deviations) of responses shown by the healthy subjects. The difference in response between addicts (mean = 0.56 mm) and healthy subjects (mean = −0.02 mm) was highly significant ($P<0.001$).

Among the opiate addicts, no significant relationship was found between the amplitude of the mydriatic response, the patient's sex or age, the daily dose of methadone, the resting pupil diameter, or the known duration of treatment. Patients receiving other drug treatments in addition to their methadone had a smaller mean naloxone response than those on methadone alone (0.36 v 0.60 mm, $F=5.023$, $P<0.05$). In 15 patients who were tested, opiate

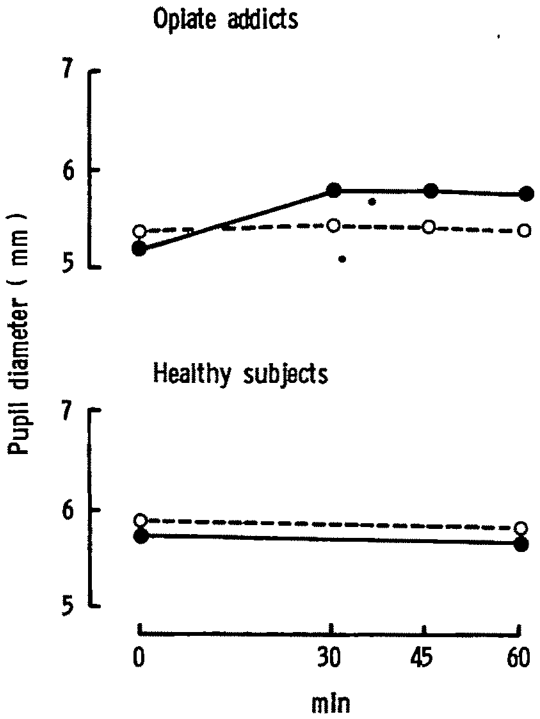

FIG. 1 Mean pupil diameters of opiate addicts and healthy subjects following instillation of naloxone eyedrops 1 mg/ml. Treated eye (●). Consensual eye (○).

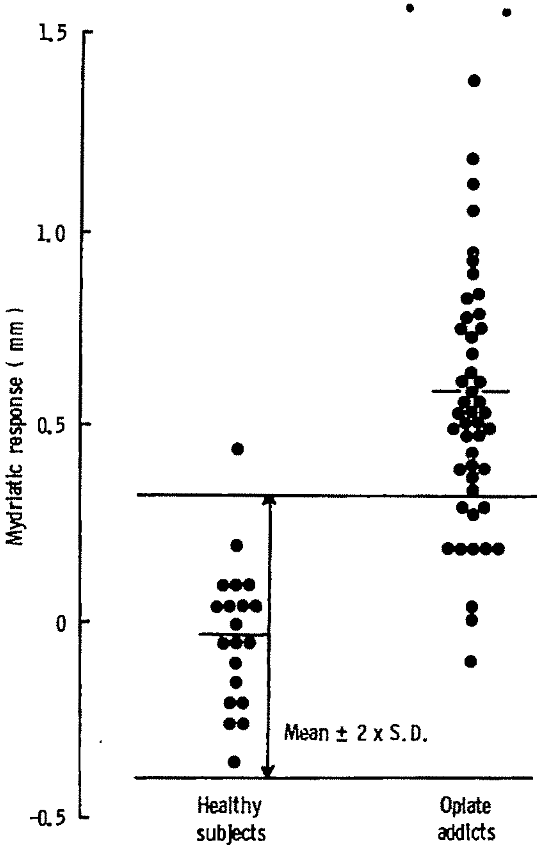

FIG. 2 Pupil diameter change in healthy subjects and opiate addicts following topical instillation of naloxone eyedrops 1 mg/ml. Horizontal lines indicated the range (mean ± 2×SD) of the normal response.

withdrawal items in the self-assessment questionnaire yielded marginally lower mean scores after than before naloxone treatment (52 v 57, $0.1>P>0.05$), thus denying any withdrawal effects of the treatment.

The naloxone responses of 12 patients who were re-tested after cessation of methadone treatment were significantly smaller than during treatment ($P<0.001$). Eleven of the 12 values obtained were within the normal range (Figure 3).

Discussion

Topical naloxone produced a mydriatic response in 36 out of 47 patients on maintenance methadone therapy. The failure of the remainder to respond is not explained easily, but in some instances may have been related to ancillary drug treatments which they were receiving at the time.

In the whole group of patients, the magnitude of the mydriatic response was such that in only 30 (those showing a diameter change of at least 0.5 mm) would the changes have been detectable under clinic conditions. The test is therefore likely to yield a high proportion of false negative results, if used as a diagnostic procedure. On the other hand, measurements on the healthy subjects suggest that there would be no false positive results.

Re-testing a group of 12 patients after withdrawal of methadone treatment was associated with loss of the naloxone response. This suggests that a positive response can be expected only when methadone is present in pharmacologically active concentrations. The test, therefore, may have some use in drug dependence treatment clinics in helping to detect current opioid influence and possibly opioid dependence.

Among patients whose pupils dilated to topical naloxone, none showed a consensual drug response, which indicates that the action was exerted locally and not systemically via drug absorption. Our findings therefore confirm the very limited previously published observations, and together are highly

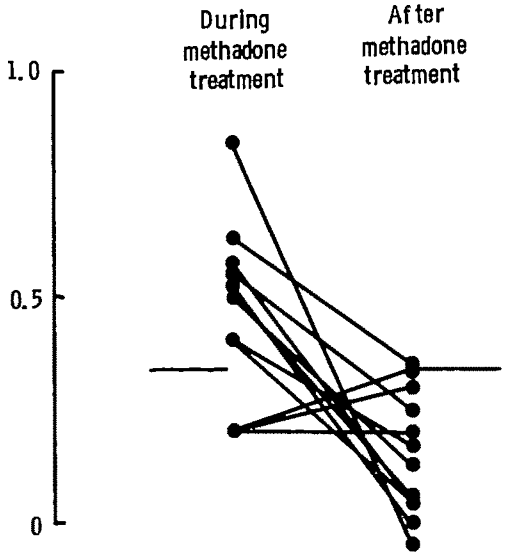

FIG. 3 Pupil diameter changes in 12 opiate addicts following topical instillation of naloxone eyedrops 1 mg/ml during methadone treatment and after withdrawal. Horizontal line indicates upper limit of normal range (Fig. 2).

suggestive of the presence of opiate receptors in the anterior uvea.

The mode of action of opiates on the pupil appears to be more complex than has been realised in the past, and probably involves both central and peripheral components. The nature of the peripheral component is unknown at present, but it is likely to arise from a reduction in release of transmitters from sympathetic nerve endings in the dilator pupillae. Blockade of these by naloxone would then result in an increase in noradrenaline release, causing the mydriasis. Such an action would be consistent with that on other tissues in experimental animals (Cairnie *et al*, 1961).

Acknowledgements

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A. H. Ghodse, MD, *Consultant Psychiatrist*

T. H. Bewley, MD, *Consultant Psychiatrist*

M. K. Kearney, MRCP, *Research Fellow, Terminal Care Support Team*

*S. E. Smith, DM, *Professor of Applied Pharmacology and Therapeutics, St. Thomas's Hospital Medical School (UMDS), London SE1 7EH.*

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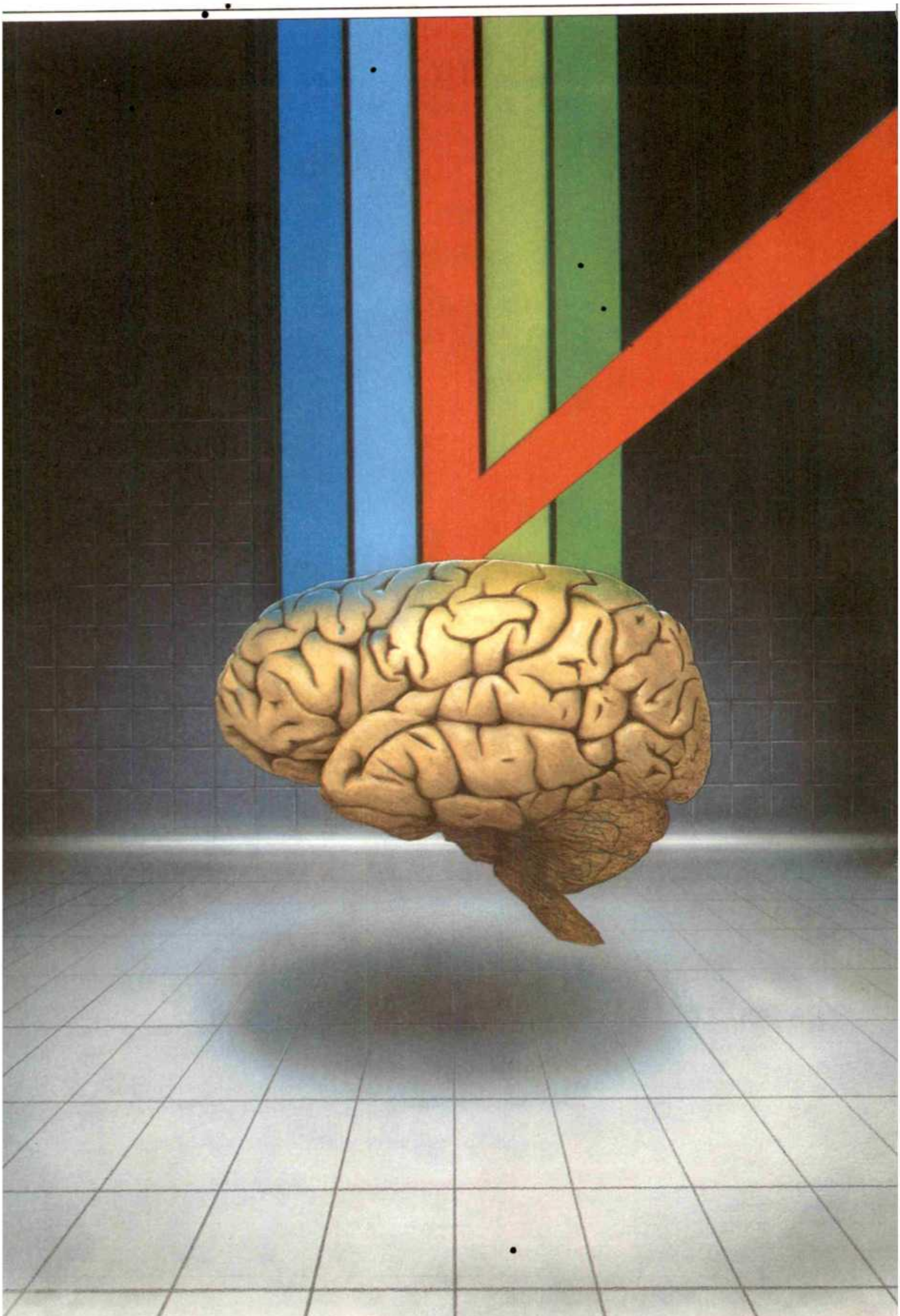

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Neuroleptic Malignant Syndrome

R. J. ABBOTT and L. A. LOIZOU

The neuroleptic malignant syndrome (NMS) occurs as a hypersensitivity response in certain patients exposed to neuroleptics. It is a relatively rare, but potentially lethal complication, the incidence of which may have been underestimated. Recent interest in NMS has arisen due to the recognition that specific therapy may now be available. This review summarises the clinical features and discusses recent ideas regarding aetiology and treatment.

Neuroleptics were first used in the treatment of psychiatric disorders in the 1950s and their side-effects are generally well recognised (Marsden & Jenner, 1980). Preston (1959) first described the clinical features of an uncommon hypersensitivity reaction to neuroleptics, which subsequently became known as the neuroleptic malignant syndrome (NMS). This term was first introduced into the English literature by Delay & Deniker (1968), although a similar syndrome, the syndrome "Neurovegatif malin" was at that time well recognised in France (Delay *et al*, 1969). Sporadic reports have since occurred from other countries (Itoh *et al*, 1977; Singh, 1981) and considerable interest in this disorder arose in America following a major review by Caroff in 1980. Reference to NMS in the UK literature is sparse, although two recent editorials (Lancet, 1984; Szabadi, 1984) indicate an increasing awareness of its importance. Allan & White (1972) described hypothalamic side-effects of phenothiazines in 1972, but the first case report which recognised NMS did not appear until 1983 (Cope & Gregg, 1983). Clough (1983) subsequently described a further case, and suggested that the disorder was more common than has generally been accepted. Until recently, no specific treatment was available for NMS, which carries a mortality of about 20%.

Incidence

The incidence of NMS is unknown, since no major series has been described, but in a review of 60 cases in the world literature, Caroff (1980) quoted an age-range of 3 to 61, with 80% under the age of 40, and a male to female ratio of 2:1. He regarded this condition as a "neglected clinical problem of major proportions", which "may be unrecognised and underdiagnosed." Delay & Deniker (1968) estimated the incidence to be 0.5 to 1% in patients taking neuroleptics. On the other hand, Baastrup *et al* (1976) described 425 patients taking a combination of haloperidol and lithium, none of whom developed NMS. Singh (1981) treated 1,500 patients over a six-year period with neuroleptics, and observed three cases—an incidence of 0.2%, while Itoh *et al* (1977) collected the largest series yet reported, 14 cases in five years. Of these patients, the majority developed symptoms shortly after the initiation or alteration of neuroleptic therapy.

Aetiology

NMS appears to be an idiosyncratic reaction to a therapeutic dose of the neuroleptic, and it has been suggested that its appearance relates to a critical level of the drug in a predisposed patient (Caroff, 1980). The symptoms may develop at a variable interval, from a few days to a number of weeks, following introduction of therapy, and clinical features usually progress over a period of 24–72 hours after onset. They tend to subside 5–10 days later, when related to oral preparations, and 10–21 days after long-acting phenothiazines (Smego & Durack, 1982). Allan & White (1972) reported that the reduction in clinical signs coincided with a fall in the urinary concentration of fluphenazine breakdown products. Re-exposure of the patient to the same neuroleptic, following recovery, may or may not result in recurrence of symptoms, suggesting that variables other than the neuroleptic drug alone may be involved (Smego & Durack, 1982).

NMS has been reported following the use of a large number of different neuroleptics, used alone or in combination with other agents such as lithium and tricyclic antidepressants (Smego & Durack, 1982). It has also been described after dopamine-depleting drugs, such as tetrabenazine and alpha-methyltyrosine (Burke *et al*, 1981). It is not specific to patients treated for psychiatric disorders since it has also occurred in Huntington's disease (Burke *et al*, 1981), pre-induction anaesthesia (Haberman, 1978), hypnotic withdrawal (Greenblatt *et al*, 1978) and in a non-psychotic child (Shields & Bray, 1976). NMS may also occur following withdrawal of drugs such as levodopa and amantadine, whose effects enhance central dopaminergic neurotransmission (Toru *et al*, 1977; Simpson & Davis, 1984).

Caroff (1980) suggested that organic brain disease might be a predisposing factor, since 11 out of 60 patients with NMS had either brain damage or a history of alcohol or drug abuse prior to neuroleptic exposure. The potential of a phenothiazine for producing the syndrome appears to parallel the antidopaminergic potency of the drug administered (Itoh *et al*, 1977).

Clinical features

The cardinal clinical features of NMS are the development of hyperthermia, muscle rigidity, and autonomic instability in a patient exposed to neuroleptics; this can best be described by reference to a patient seen recently. A 26-year-old female presented with a four-day history of acute psychiatric disturbance, which developed on a background of normal personality, except for a short period of panic attacks three years previously. In the four days prior to her admission, she had initially become withdrawn, then restless and agitated, did not sleep, developed visual and auditory hallucinations, and became suspicious of her relatives. On admission to the psychiatric unit, she was noted to be disorientated in space and time, had no insight into her condition, and was uncooperative, with incoherent speech. There were no focal neurological signs and general examination was normal. There was no evidence of systemic disorder or alcoholic abuse to indicate a possible organic toxic confusional state, and the initial diagnosis was of a functional psychosis related to acute emotional stress. She was treated with lorazepam, 2.5 mgs, tds; temazepam, 20 mgs, nocte, and chlorpromazine, 100 mgs intramuscularly for three days. Following the third dose of chlorpromazine, she developed a temperature of 38°C and became drowsy. Tone in the limbs was normal at this stage. Investigations showed an ESR of 33 mm in the first hour, normal CT brain scan and CSF examination, but an abnormal EEG, with a diffuse mixture of fast and slow rhythms. The chlorpromazine was discontinued. Over the succeeding four days, the pyrexia increased to 39.5°C and she developed sweating, tachycardia (120 per minute), and tachypnoea. She became more unresponsive, requiring nasogastric-feeding and bladder catheterisation. Choreiform movements of the limbs and face became prominent, but there were no long-tract neurological signs. Catatonia due to a psychosis was considered and she was given two ECTs; following the second treatment, she was able to understand commands and to walk with help. Chlorpromazine, 100 mgs orally was then administered daily for three days and trifluoperazine, 10 mgs orally, daily for a further five days. She again deteriorated, becoming pyrexial, almost totally unrousable, and mute, with gross generalised rigidity, bilateral divergent squint, sluggish reflexes, and continuous choreiform movements of the limbs. A repeat CT scan and CSF examination were again normal, but the EEG remained diffusely abnormal. There was a neutrophil leucocytosis and elevation of hepatic transaminases. She was treated with procyclidine and cooling, and neuroleptics were stopped. Over the following four days, she showed profound bradykinesia and rigidity, involuntary choreiform movements, and subsequently catatonic posturing. However, her conscious level and responsiveness improved and the pyrexia resolved. She was then prompted to get up and walk, and within a week was fully recovered, except for having no recollection of the events of the six weeks of her illness. She remains well, 14 months later, on no medication.

This patient displayed the typical features of extrapyramidal rigidity of a plastic type, which occurs in NMS associated with bradykinesia and jerky involuntary movements, which are a frequent accompaniment in this condition. Catatonic features became prominent as the disorder developed, along with mutism and posturing, and the conscious level rapidly became depressed, though Smego & Durack (1982) have suggested that alertness and cooperation are often retained in the early stages of NMS. This patient at no stage developed the pulmonary congestion which was originally described as a cardinal feature of NMS (Delay & Deniker, 1968), but it now seems likely that this is a secondary complication.

The diagnosis of NMS is made on clinical grounds, since laboratory investigations show secondary or non-specific changes only. Thus, a neutrophil leucocytosis occurs without evidence of infection, and liver transaminases may be elevated. A rise in creatine phosphokinase (CPK) and serum potassium are indices of skeletal muscle necrosis. The EEG may show non-specific slow wave abnormalities, but CT brain scans and CSF examination are invariably negative. Postmortem studies (Morris *et al*, 1980; Cope & Gregg, 1983) have shown normal brain morphology and no site of systemic infection.

Differential diagnosis

Smego & Durack (1982) suggest that NMS should be included in the differential diagnosis of any febrile patient with a history of neuroleptic ingestion.

Clearly, infections involving the central nervous system, such as encephalitis, meningitis, or tetanus, must be excluded, as must extrapyramidal disorders, such as severe Parkinson's disease and the rigid form of Huntington's chorea. Akinetic mutism, the 'locked in' syndrome, and other disorders involving higher centres or the brainstem should be excluded by a careful neurological examination. Other conditions which give rise to catatonia (Gelenberg, 1967) should also be considered.

More difficult to exclude are the less common disorders which produce hyperpyrexia with varying degrees of hypertonia. Heat stroke occurs in the presence of high ambient temperatures, and a number of fatalities have occurred in patients taking phenothiazines in such conditions (Ayd, 1956; Zelman & Guillan, 1970). Muscle rigidity is not usually a prominent feature of this condition, however.

Stauder's lethal catatonia (Stauder, 1934; Billing & Freeman, 1943) was described many years before neuroleptics were introduced, and is clinically indistinguishable from NMS, though the pathophysiological relationship between these two conditions is unclear. It is usually preceded by a prodromal phase lasting 1–2 weeks, following which the patient displays features of anxiety and restlessness; sudden clinical deterioration then occurs, the conscious level decreases, body temperature rises dramatically, and vasomotor collapse ensues. Postmortem studies have revealed small discrete haemorrhages in the hypothalamus and pituitary (Billing & Freeman, 1943).

Malignant hyperpyrexia is a hypersensitivity reaction which occurs in genetically predisposed individuals who are exposed to certain anaesthetics (Gronert, 1980). The underlying abnormality lies within skeletal muscle, and the condition is characterised by the development of intense muscle spasm and hyperpyrexia, within minutes of anaesthetic induction. There is often a positive family history, and it carries a 70% mortality. Although an association between malignant hyperpyrexia and NMS has not been definitively established, Caroff *et al* (1983) demonstrated that striated muscle from a patient who had recovered from NMS showed a response diagnostic of the susceptibility to malignant hyperpyrexia, when exposed to halothane *in vitro*.

Conversely, Denborough *et al* (1984) described the occurrence of NMS following treatment with fluphenazine in a patient with the muscle disorder which predisposes to malignant hyperpyrexia. In a clinical context, however, diagnostic confusion between these two disorders should not occur, since the pattern of clinical presentation of each is distinct.

Pathophysiology

It is widely recognised that phenothiazines may reduce body temperature and that hypothermia may be a complication of their use (Exton Smith, 1972). They have been used to treat life-threatening hyperpyrexia due to heat stroke (Hoagland & Bishop, 1961), yet the sites and mechanisms of their thermoregulating action in man are largely unknown. Animal experiments have demonstrated considerable variation in thermo-regulatory response to neuroleptics, depending upon the species studied and the site of drug administration. Thus, both rats (Hofmann & Zarrow, 1958) and monkeys (Chai *et al*, 1976) show a precipitous fall in body temperature when chlorpromazine is injected subcutaneously, whereas, when injected directly into the rostral hypothalamus or third ventricle of the rat, it produces prolonged *hyperthermia* (Rewerski & Jori, 1968). Further animal studies have demonstrated variation in thermo-regulatory response to phenothiazines, depending upon the age, sex, and social conditions of the animals (Barbelby & Loepfe Hinkaanen, 1979).

In man, it has been suggested that certain combinations of factors become operative in rendering an individual susceptible to NMS at any given time (Caroff, 1980); e.g. Itoh *et al* (1977) found that exhaustion and dehydration were commonly present at the initiation of phenothiazine therapy. Debate has arisen as to whether the muscle rigidity and hyperpyrexia originate from an effect of the central action of drugs, or are due to a peripheral effect within skeletal muscle. In malignant hyperpyrexia, where the primary disorder lies within the muscle tissue, the extreme spasm of the muscles is sufficient to generate a dramatic rise in body temperature, and a similar mechanism has been considered for NMS. The evidence for this belief was provided by *in vitro* studies on muscle biopsy specimens (Caroff *et al*, 1983; Denborough *et al*, 1984). Further evidence comes from the effect of dantrolene, a drug acting peripherally on skeletal muscle, which produced a rapid relaxation in muscle tone in a patient with NMS and a coincidental fall in body temperature from 42°C to normal (Goulon *et al*, 1983). Granato *et al* (1983) found that dantrolene normalised body temperature within 12 hours of administration and that the elevated CPK fell within 48 hours, but their patient remained rigid, tremulous, and stuporose until bromocriptine, a central acting dopamine receptor agonist, was given five days later.

Morris *et al* (1980), in contrast, favoured a central mechanism for both the pyrexia and rigidity since curare—a neuromuscular blocker—produced complete flaccidity in a case of NMS, an effect not seen in malignant hyperpyrexia. The pyrexia improved slightly following muscle relaxation, but did not normalise for a further 19 days. In the patient described above, pyrexia was an early feature, in association with stupor and autonomic signs. Muscle rigidity only developed at a later stage, suggesting that at least in the early stages of this condition, the hyperpyrexia has a central origin, and probably arises from an effect upon the hypothalamic thermo-regulatory centres.

Treatment

Until recently, the management of established NMS has relied upon supportive therapy for the cardio-respiratory complications. It is clearly imperative that neuroleptics are stopped immediately the condition is suspected; strenuous attempts must be made to reduce the body temperature, respiratory support may be required via artificial ventilation, and secondary infections will require antibiotics. Renal dialysis has been described in a patient who developed acute renal failure secondary to widespread rhabdomyolysis (Samii *et al*, 1976), but is not effective in removing circulating neuroleptics, which are protein and lipid-bound (Caroff, 1980). More specific measures aimed at reducing muscle tone have included anticholinergics, but these drugs are generally regarded as ineffective (Itoh *et al*, 1977). ECT also was ineffective in two patients, one of whom had a cardiac arrest during the procedure (Regestein *et al*, 1977).

There are recent reports of two separate lines of treatment, which may be complementary. Since blockade of hypothalamic dopamine receptors by neuroleptics is the probable initiating mechanism, the effects of drugs which facilitate central dopaminergic mechanisms have been studied. Limited success was achieved with amantadine (McCarron *et al*, 1982; Gelenberg & Mandel, 1977) but more recently bromocriptine, in a daily dose of 60 mg, was shown effectively to reduce muscle tone and to improve conscious level (Granato *et al*, 1983; Mueller *et al*, 1983). The complementary use of dantrolene (10 mg/kg) to reduce muscle tone by a peripheral effect has been demonstrated on a number of occasions (Delacour *et al*, 1981; Boles *et al*, 1982; Coons *et al*, 1982; Goekopp & Carbaat, 1982; Goulon *et al*, 1983; Granato *et al*, 1983; May *et al*, 1983) and at present, the best drug treatment for NMS appears to be a combination of bromocriptine and dantrolene.

Conclusions

Much remains to be learned about the conditions which lead to the development of NMS, which, although a relatively rare complication of neuroleptic therapy, has perhaps been underestimated in incidence. There is a need for caution when using potent neuroleptics, and the combination of a greater awareness of this condition with the development of more specific forms of treatment may lead to future improvements in the prognosis. Delay & Deniker (1968) in their original description of this condition provide the most practical advice for the clinician: "should a fever commence and be recorded on two successive occasions one must stop medication immediately and completely, especially when there is no obvious infectious cause for the fever."

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*R. J. Abbott, MD, MRCP, *Senior Registrar in Neurology, Pinderfields General Hospital, Wakefield.*

L. A. Loizou, PhD, MRCP, *Consultant Neurologist, Pinderfields General Hospital, Wakefield.*

*Correspondence: *St. James's University Hospital, Beckett Street, Leeds 9.*

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Imipramine and Amitriptyline Plasma Concentrations and Clinical Response in Major Depression

JAMES H. KOCSIS, ISRAEL HANIN, CHARLES BOWDEN and DAVID BRUNSWICK

Plasma drug concentrations and clinical response were measured in two groups of hospitalised depressed patients, who received amitriptyline or imipramine double-blind, in a dosage of 250 mg for four weeks. Virtually no significant linear or curvilinear relationships were found between any plasma measure and any measure of clinical response. Modest but significant direct relationships were found between age and concentration of parent drugs but not demethylated metabolites. Blood drug level measurement therefore appears to be of little value in monitoring drug treatment of depressed in-patients.

The efficacy of tricyclic antidepressants (TCAs) in treating depressive symptoms has been repeatedly documented (Cole & Davis, 1975), but complete or partial therapeutic failure is not uncommon. Reasons for this include patients' diagnostic heterogeneity and inter-individual differences in the metabolism of these drugs. Steady-state plasma TCA concentrations are low (nanogram range), require sensitive chemical measurement, and vary widely among individuals. Variability in steady-state plasma levels is presumed to extend to tissue concentrations at pharmocological sites of antidepressant action and might constitute an important factor in determining clinical response.

As the value of plasma level measurements has been shown for several drugs (e.g. Phenytoin, digitalis, lithium), factors contributing to inter-individual differences in steady-state TCA plasma concentrations and the relationship of these measurements to clinical antidepressant efficacy have been investigated. Results so far support Åsberg's contentions that plasma TCA concentrations relate to clinical antidepressant effect in a complex way, and that there is variability in these relationships among these drugs (Åsberg, 1974). Studies of relationships between imipramine (IMI) plus its demethylated metabolite desmethylimipramine (DMI) and clinical response have generally supported a sigmoidal relationship with thresholds for optimal response in the 150–250 ng/ml range and no upper limit beyond which clinical response falls off (Olivier-Martin *et al*, 1975; Reisby *et al*, 1977; Glassman *et al*, 1977), but one recent study has failed to confirm this (Simpson *et al*, 1982). Studies concerning amitriptyline (AMI) plasma levels and its demethylated metabolite nortriptyline (NOR), in relationship to clinical response have been inconclusive. Some studies have found linear relationships (Braithwaite *et al*, 1972; Montgomery & Braithwaite, 1975; Ziegler *et al*, 1976; Kupfer *et al*, 1977), while others have reported inverted-U or 'therapeutic window' relationships (Breyer *et al*, 1982), and some have found no relationship at all (Coppen *et al*, 1978; Robinson *et al*, 1979; Liisberg *et al*, 1978; Mendelwicz *et al*, 1980).

Because tertiary tricyclics such as IMI and AMI are demethylated to corresponding secondary amines *in vivo*, patients have drug effects from active metabolites (DMI and NOR respectively) as well as from parent compounds, and sometimes the concentrations of the metabolite predominate at steady-state levels. Whether clinical response is affected by steady-state concentrations of parent drug or metabolite separately or by the sum or the ratio of the two is still unclear; one study found that clinical responses to AMI was correlated specifically with the NOR/AMI ratio and not with the sum or individual levels of parent drug or metabolite (Jungkunz & Kuss, 1978).

Several factors have been found to alter pharmacokinetic properties of TCAs, thus affecting plasma and tissue concentrations. A major source of this variability stems from inter-individual differences in the acvitity of hepatic microsomal enzymes which are responsible for their biodegradation. Microsomal enzyme activity, while largely genetically determined, may also be influenced by other factors such as age and concomitant drug ingestion (Glassman & Perel, 1973; Jungkunz & Kuss, 1978). Relationships between dose of medication and steady-state plasma concentrations may therefore vary in clinically important ways under a variety of influences.

This paper reports a series of plasma TCA determinations and their relationships with therapeutic efficacy. Hospitalised depressed patients included in this study were treated in a double-blind fashion with either AMI or IMI.

Method

The design and rationale of the NIMH-CRB Collaborative Program—Psychobiology of Depression—Biological Study have been described earlier (Maas *et al*, 1980; Secunda *et al*, 1980; Katz *et al*, 1984). Data were obtained from 90 patients with Major Depressive Disorder, who were hospitalised at one of six university hospitals which made up the Collaborative Study. Fifty-nine patients were diagnosed as unipolar (27 males, 32 females, mean Hamilton Score 29±10), and 31 were bipolar (21 males, 10 females, mean Hamilton Score 26±8). The approximately equal sex distribution of subjects in this study was selected because of concomitant biological studies, but did not reflect that of the naturally presenting depressed population in the collaborating centres.

Diagnoses were made using the Schedule for Affective Disorders and Schizophrenia (SADS), a structured clinical interview, and Research Diagnostic Criteria (RDC) (Spitzer *et al*, 1978)—a set of operational criteria for psychiatric diagnoses using data derived from the SADS interview. Eighty-five percent of subjects met criteria for the RDC Endogenous sub-type and 15% met criteria for the Psychotic sub-type. Patients having major medical disorders were excluded. Concomitant medication use was restricted to occasional chloral hydrate, aspirin, or non-absorbable cathartics or faecal softeners.

The first two weeks in hospital constituted a drug-free, baseline period, with placebo given on days 3–14; active drug therapy was initiated on day 15. Fifty-mg capsules were used along with matching placebo, which was given three times per day to correspond with the timing of administration of active medication (0900, 1700, 2100 hours). Patients were assigned randomly to either AMI or IMI, using a double-blind procedure. Drugs were given in divided doses and continued until day 41 according to the following schedule: Day 15+16—100 mg, Day 17+8—150 mg, Day 19+20—200 mg, Day 21–41—250 mg. If side-effects occured prior to Day 25, doses were adjusted as clinically indicated, but every effort was made to achieve maximal dose. Patients who could not be maintained on a fixed dose after Day 25 were dropped from the study, patients who improved on placebo (i.e., Hamilton score less than 16) were also dropped.

Of 132 depressed patients who entered the study, 23 dropped out because of side-effects (AMI = 4, IMI = 4), non-compliance (AMI = 3, IMI = 6), clinical worsening (AMI = 2, IMI = 2), or intercurrent medical illness (AMI = 1, IMI = 1). Three dropouts occurred during the baseline placebo washout, nine during AMI treatment, and 11 during IMI treatment. For technical reasons, 19 patients had no blood data. Twelve patients (AMI = 8, IMI = 4) required treatment at reduced doses (150–200 mg) because of side-effects; the remaining 78 received a fixed dose of 250 mg for at least three weeks. Plasma drug concentration data from these 90 who completed the study constitute the basis of this report.

Behavioural change and outcome measures: Multiple change and outcome measures were performed, and are described more fully in Katz *et al* (1984). These measures included the 24-item version of the Hamilton Depression Scale (HAM-D) (Hamilton, 1960) and the Global Assessment Scale (GAS) (Spitzer & Endicott, 1973) performed by trained psychiatric raters, and two outcome constructs—the Depressed State Construct (DSC) and the Global Improvement Construct (GIC). The categorical outcome (OUTCAT) is derived from the Ham-D, Itil-Katz global scales (Secunda *et al*, 1980), and the GAS; its scores range from 1–6, with 1 or 2 = Recovered, 5 or 6 = Not recovered, and 3–4 reflecting indeterminate levels of outcome. Because of reports that linear plasma level-response relationships may exist only in certain depressive sub-types (Glassman *et al*, 1977; Bech, 1981), we analysed our data separately for such relationships in the following subgroups of our total patient sample: unipolars, bipolars, males, females, RDC endogenous, Newcastle endogenous (Bech, 1981) and RDC non-psychotic.

Sample collection: Blood samples were drawn in the morning prior to administration of medication or meals, on days 10, 22, 28, 29, 33, 34, 35 and 41 of study using heparinised Vacutainer R tubes in the first 21 subjects (AMI = 9, IMI = 12) and heparinised glass syringes in the remaining 69. Blood was promptly transferred to a centrifuge tube in an icebath. Following centrifugation (1600 Xg for 15 minutes) in a refrigerated centrifuge a 3 ml aliquot of plasma was transferred into each of two clean culture tubes in an icebath. These tubes were capped with Teflon, labelled, and stored at −70 degrees C until shipment to a single centre for assay. Samples were analysed in duplicate and double-blind, using a gas chromatography mass spectrometric method (Biggs *et al*, 1976). The drugs were extracted from basic solution with petroleum ether and the secondary amines (NT+DMI) derivatised with trifluoroacetic anhydride. Selected Ion Monitoring analyses were carried out on a Finnigan 3200 Gas Chromatograph/Mass Spectrometer interfaced with a Computer Automation LSI computer, using the Washington University Spectrometry Center program system. Steady state plasma measures were computed by averaging day 33, 34, 35, and 41 determinations for each measure.

Because of previous reports of effects of contact with heparinised Vacutainer R tubes on plasma concentrations (Brunswick & Mendels, 1977; Cochran *et al*, 1978), we identified the 21 cases in which these were used, and calculated their steady-state drug and metabolite means. We matched this group with a sample from the remainder on diagnosis, drug, sex, dose, age, weight and outcome. We then compared distributions of these two drugs separately on drug, metabolite, total, and metabolite-to-drug ratio, using the Kolmolgorov 2-sample test. No significant differences were found between samples exposed to Vacutainer R tubes and those obtained in glass syringes; therefore, we performed our statistical analyses on the entire patient sample.

Data Analyses The distribution of both raw and log transformed plasma level measures was examined separately by sex and diagnostic group. In most cases log-transformed data fit a normal distribution better, and were used for further analyses. T-tests, Pearson correlation coefficients, and analysis of covariance were used to analyse relationships between outcome measures and drug concentration, metabolite concentration, sum of drug plus metabolite and metabolite to drug ratio for both AMI and IMI. Pearson correlation coefficients were also computed between age and drug, metabolite, total drug plus metabolite concentrations, and metabolite/drug ratio.

Results

Age, Sex and Center Effects

Correlations between age and various plasma drug measures are summarised in Table I. Parent drug concentrations (AMI, IMI) and age were found to correlate positively, in a modest but significant way, for both drugs. No significant correlations were found between metabolite (NOR, DMI) concentrations and age.

Analysis of variance, followed by Duncan Multiple Range Tests were performed to examine effects of sex and centre on the various plasma measures. No significant sex effects were found for either drug. Two centre effects were found for AMI, where San Antonio had significantly lower metabolite and total concentration in comparison to the other five centres, none of which differed significantly. Because of age effects on plasma drug measures, analyses of relationships between categorical outcome and plasma measures, described below, were all undertaken, with age as a covariate. In no instance was significance of relationships altered by the covariant analysis.

Outcome

In general, outcome for patients treated in this study was favourable and similar to other studies involving inpatients (Olivier-Martin *et al*, 1975; Reisby *et al*, 1977; Glassman *et al*, 1977; Kupfer *et al*, 1977; Coppen *et al*, 1978). Table II shows the distribution of categorical outcomes for the two drug treatments. Forty-seven percent of AMI and 46% of IMI treated patients were rated as recovered (OUTCAT 1 or 2), whereas 24% of AMI-treated and 21% of IMI-treated patients were classified as poor responders (OUTCAT 5 or 6). The remaining patients had indeterminate responses (OUTCAT 3 or 4).

TABLE I

*Pearson correlation coefficients between age and plasma drug measures**

Measure	*AMI* r	*AMI* *P*	*IMI* r	*IMI* *P*
Log drug level	.41	.007	.37	.028
Log metabolite level	.17	NS	.17	NS
Log total level	.35	.02	.33	.56
Log ratio (Metabolite/Drug)	−.31	.043	−.17	NS

*Includes full-dose patients only AMI = 43, IMI = 35

TABLE II

Distribution of categorical outcome (OUTCAT) for two days

Outcome (rating)	*Drug* *AMI* *n* (%)	*IMI* *n* (%)
Recovered (OUTCAT 1 or 2)	24 (47)	18 (46)
Intermediate (OUTCAT 3 or 4)	10 (10)	13 (33)
Non-recovered (OUTCAT 3 or 4)	12 (24)	8 (21)
Unknown	5 (10)	0 (0)
Total *n*	51 (100)	39 (100)

Steady-state plasma drug measures achieved by study patients are summarised in Table III. Mean total concentrations for AMI and IMI were 310 and 293 ng/ml, respectively, (S.D. for AMI and IMI, 135 and 168 ng/ml, respectively). Few patients achieved low levels, only 5/51 AMI patients and 4/39 IMI patients having steady-state total concentrations below 150 ng/ml. Plasma drug measures in the small numbers of patients who required reduced doses at steady-state (AMI = 8, IMI = 4) did not differ significantly from full-dose patients, with only one exception. Reduced dose AMI patients had significantly lower metabolite concentrations, but did not differ significantly in measures of parent compound or total of drug-plus-metabolite.

Relationships between mean steady-state plasma drug measures and Day 40 behavioural change and outcome measures were analysed separately for the total depressed sample and for the various depressive sub-groups (bipolar, unipolar, male, female, Newcastle endogenous, RDC endogenous, and RDC non-psychotic). Outcome measures included the final HAM-D score, the HAM-D change score (Day 40 minus Day 10), the GAS change score, the OUTCAT score, the day 40 GIC score, and the Day 40 DSC score. Scatter plots were generated in each instance (e.g. Figs. 1 & 2) between a particular outcome measure and each plasma drug measures, i.e., drug concentration, metabolite concentration, total concentration, and ratio. (These plots are available from the first author upon request.) Correlation coefficients were done to analyse these relationships and, with only one exception, all were non-significant. Females treated with IMI showed

TABLE III

Mean steady-state plasma measures

Measure	*AMI* *X±S.D.*	*IMI* *X±S.D.*
Drug concentration (ng/ml)	159±80	125±76
Metabolite concentration (ng/ml)	150±71	168±126
Total drug + metabolite (ng/ml)	310±135	293±168
Ratio (metabolite/drug)	1.05±0.48	1.63±1.13

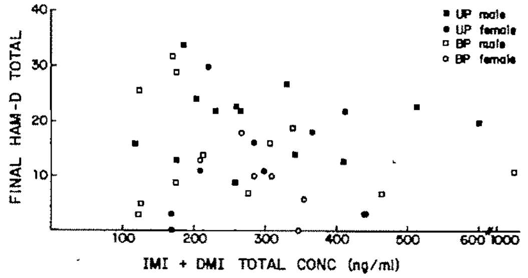

FIG. 1 Relationship between final HAM-D scores and IMI + DMI total concentration

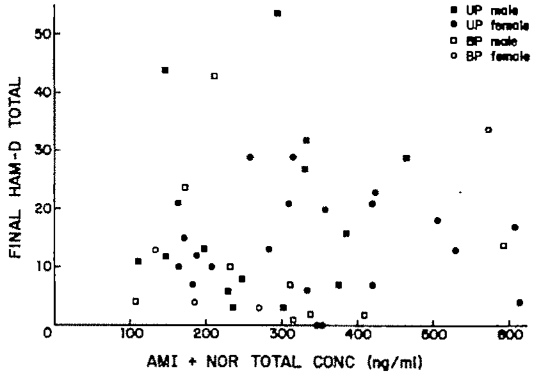

FIG. 2 Relationship between final HAM-D scores and AMI + NOR total concentration

a significant inverse correlation between metabolite/drug ratio and OUTCAT ($r = .6$, $P = .02$). Covariant analyses to correct for age effects were performed, as well as t-tests, were performed comparing each plasma measure between good (OUTCAT 1 or 2) and poor (OUTCAT 5 or 6) outcome patients. These were non-significant in all instances.

To inspect the data for possible curvilinear relationships (e.g., sigmoid or inverted-U), contingency tables were made of outcome above and below the median values of all plasma measures, as well as of upper, middle, and lower thirds of values for both drugs. None of these distributions proved to be significantly skewed when examined using chi square analyses.

Discussion

This study did not find evidence of either linear or curvilinear relationships between plasma total concentration (parent drug plus metabolite) and any one of several measures of clinical outcome for hospitalised patients with Major Depressive Disorders, who had been treated for four weeks with either IMI or AMI. Separate analyses were also performed which examined other drug measures (parent drug, metabolite, ratio) for relationships to clinical response. These revealed only one significant association: females treated with IMI were found to have a significant inverse correlation between DMI/IMI ratio and categorical outcome. However, this may be a chance finding, as a large number of correlations were performed. These results are consistent with those previously reported by the WHO Collaborative Group (Coppen *et al*, 1978), and with three other studies (Robinson *et al*, 1979; Liisberg *et al*, 1978; Mendelwicz *et al*, 1980) which did not find plasma level relationships to clinical response for AMI. However, current findings are at variance with prior reports which have found direct or inverted-U relationships between total concentration of AMI and clinical outcome (Braithwaite *et al*, 1972; Montgomery & Braithwaite, 1975; Ziegler *et al*, 1976; Kupfer *et al*, 1977; Breyer *et al*, 1982). Results with IMI concentrations reported here also fail to confirm a number of earlier reports of direct or sigmoidal relationships between total (IMI plus DMI) concentrations and clinical response (Olivier-Martin *et al*, 1975; Reisby *et al*, 1977; Glassman *et al*, 1977).

When linear or curvilinear relationships between plasma concentrations of drug and clinical response are not found, one possible explanation may be diagnostic heterogeneity in patient samples, with inclusion of many treatment resistant cases (Friedel, 1982). However, assessing the current study, it should be noted that the patient sample was largely endogenous and nondelusional and thus likely to respond to TCAs. In addition, the lack of relationships persisted when non-endogenous and psychotic patients were excluded from the analyses, while the overall rate of treatment response was comparable to other studies involving in-patients which have reported such relationships. Therefore, the lack of observable relationships does not appear to reflect an atypical patient sample.

The current study contained a somewhat unusual sex distribution, in that the female:male ratio was 7:8 (14:25 in the IMI-treated subjects). The sample also contains a mixture of unipolar and bipolar patients. However, prior studies do not suggest that sex or polarity are important factors in determining plasma level—response relationships (Glassman *et al*, 1977; Friedel, 1982).

Another issue in evaluating our results is that, in comparison with most prior studies, a higher fixed dose (250 mg) of drug was prescribed and that higher steady-state total concentrations for both drugs resulted: few subjects in our samples, treated with either drug had steady-state totals below

150 ng/ml. Thus, interpretation of plasma concentration/response relationships at the low end of a possible therapeutic threshold value or 'therapeutic window' may be hampered by the high range of plasma concentrations achieved here. On the other hand, since we did observe large numbers of patients with totals above 300 ng/ml, and these 'high' blood concentration groups had outcomes no worse than those observed with our intermediate or low level groups, these data do speak strongly against any thresholds above which therapeutic response rates fall off with either drug. Similarly, no relationships of either a linear or inverted-U ('therapeutic window') type were observed between steady-state concentrations of demethylated metabolite (DMI, NOR) and any measure of clinical outcome. Caution should be used in comparing these results to prior studies of NOR used alone as an antidepressant, which showed an inverted-U relationship between steady-state plasma concentrations and clinical response (Åsberg *et al*, 1971), but such relationships could be altered by the simultaneous presence of significant concentrations of the parent drug.

Our study confirms previous investigations (Nies *et al*, 1977) which show direct relationships between age and TCA steady-state plasma concentrations at fixed doses; these appear to apply primarily to the parent drugs. No increase was found in steady-state concentrations of demethylated metabolites (DMI, NOR) with advancing age, consistent with prior reports that NOR metabolism is unaffected by ageing (Nies *et al*, 1977; Friedel, 1982) and that hepatic demethylating enzymes are more affected by ageing than the cytochrome oxidase system. Older patients, who are particularly susceptible to TCA side-effects and toxicity, may therefore benefit from more cautious dosing and blood level monitoring, when tertiary amine tricyclics are prescribed.

The results of this study did not show linear or curvilinear relationships between total plasma drug concentrations and clinical outcome in hospitalised depressed patients treated with AMI or IMI at 250 mg/day. Under these clinical circumstances, measurement of plasma levels of these drugs appears to be of limited clinical use and may be only an expensive method of confirming that the patient has a certain minimum of drug in his system. This conclusion, however, must be qualified, in that few of our patients achieved 'low' concentrations of drug, so that measurement of drug levels of AMI or IMI may be useful in cases of drug non-response. In such instances, detection of low levels might lead to use of even higher doses, and thus enhancement of response. These possibilities were not investigated by the design of the current study, and require further research.

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*James H. Kocsis, MD, *Associate Professor of Psychiatry, Cornell Univesity Medical College, Payne Whitney Clinic, The New York Hospital, 525 East 68th Street, New York, NY 10021, USA.*

Israel Hanin, PhD, *Professor of Psychology, Pharmacology and Psychiatry, Western Psychiatric Institute and Clinic, 3811 O'Hara Street, Room 1320, Pittsburgh, Pennsylvania*

Charles Bowden, MD, *Professor of Psychiatry, Department of Psychiatry University of Texas Health Sciences Center, 7703, Floyd Curl Drive, San Antonio, Texas 78284.*

David Brunswick, PhD, *Research Associate Professor of Biochemistry in Psychiatry, Department of Psychiatry, V.A. Medical Center, University and Woodland Avenues, Philadelphia, Pennsylvania 19104.*

*Correspondence

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Raised Plasma Cortisol Concentrations a Feature of Drug-Free Psychotics and not Specific for Depression

J. E. CHRISTIE, L. J. WHALLEY, H. DICK, D. H. R. BLACKWOOD, I. M. BLACKBURN
and G. FINK

To determine whether high plasma cortisol concentrations are a distinctive feature of depression or whether plasma cortisol is also elevated in other forms of psychosis, cortisol concentrations were measured in 59 patients with acute functional psychoses, six non-psychotic depressed patients and 37 control subjects, all free of antidepressant and neuroleptic drugs for at least three months. Patients with schizo-affective disorder, manic type, had the highest concentrations throughout the day and those with major depressive disorder, psychotic sub-type had higher concentrations than controls in the afternoon and evening. Manic and schizophrenic patients had cortisol concentrations above controls in the afternoon only. Elevated concentrations were not related to the presence of depressed mood or to duration of stay in hospital, and a return to normal occurred irrespective of the type of treatment used. Thus raised plasma cortisol concentrations are a feature of psychotic illness, but in drug-free patients are not specific for severe depression.

The pituitary-adrenal cortical axis has been by far the most extensively studied endocrine system in psychiatry, increased activity has been consistently reported in depressive illness (Gibbons, 1964; Sachar, 1967; Sachar *et al*, 1973; Carpenter & Bunney, 1971; Carroll *et al*, 1976), with plasma cortisol concentrations falling to normal after successful treatment with antidepressants (Carroll *et al*, 1976) or electroconvulsive therapy (Christie *et al*, 1982). Other studies have suggested that hypercortisolaemia in depression may be associated with resistance to dexamethasone suppression (Rubin *et al*, 1980; Carroll *et al*, 1981). These findings support the hypothesis that in depression, the same abnormality of the central nervous system underlies the hypersecretion of cortisol, resistance to dexamethasone suppression and signs and symptoms of depressive illness. However, a number of recent studies have challenged the specificity of the dexamethasone suppression test (Graham *et al*, 1982; Raskind *et al*, 1982; Coppen *et al*, 1983); Stokes *et al* (1984a) have reported that non-suppression is common in manic patients and is not associated with any particular sub-type of depressive illness. There have been far fewer cross-diagnostic studies of plasma cortisol in psychiatric patients, possibly because the dexamethasone test is so much easier to complete satisfactorily, so that it cannot be stated that hypercortisolaemia is a specific feature of depressive illness.

The present study aimed to determine the diagnostic specificity of raised plasma cortisol concentrations in newly admitted psychiatric patients. There are several methodological problems in research of this type. Firstly, there is the choice of diagnostic criteria. Kendell (1982) has recommended that as diagnostic categories remain at present provisional, a variety of diagnostic criteria should be used when relating diagnostic groups to biological variables. Secondly, there is the identification of patients in sufficient numbers in each diagnostic group to allow satisfactory comparisons to be made. Thirdly, effects of hospital admission need to be distinguished from the features of illness. Next, the diagnostic groups should be comparable in terms of duration of illness, so that only acutely ill patients are included. Further, blood samples should be obtained at multiple points from an indwelling venous cannula, allowing for pulsatile release, diurnal variation and the stimulation of cortisol release by venepuncture. Finally, subjects should be free of drugs known to affect cortisol release. In view of these many difficulties it is perhaps not surprising that after some 20 years of research, it is not unequivocably established that hypercortisolaemia is a specific feature of depressive illness.

The present study was designed to meet criticisms of this work and to test the hypothesis that increased plasma cortisol concentrations are a specific feature of depression. We have studied plasma cortisol concentrations in 65 newly-admitted drug-free patients, primarily with symptoms of acute functional psychoses who were allocated to diagnostic groups according to the Research Diagnostic Criteria (RDC, Spitzer *et al*, 1978) and the criteria of Feighner *et al*(1972). The blood sampling technique, carried out through a 17 h neuroendocrine day, allowed for the diurnal and pulsatile patterns of plasma cortisol secretion. We also studied the relationship between plasma cortisol concentrations and the duration of stay in hospital before blood sampling and the changes in cortisol concentrations associated with recovery from a psychotic illness. Finally, because depressed mood is present in many patients with a psychotic illness other than depression (Wing *et al*, 1974), we examined the relationship between clinical symptoms recorded on psychiatric rating scales and plasma cortisol concentrations.

Method

Patients selection and drug exposure

Patients with symptoms suggestive of an acute psychotic illness who had been free of neuroleptic or antidepressant drugs for at least three months were selected from routine admissions to the Royal Edinburgh Hospital. The drug exposure of patients was established from the patients' self reports, from relatives, and from medical records. All patients consented to the study procedures. The 65 patients remained free of neuroleptic and antidepressant drugs for the duration of the study, but 29 required sedation (25 amylobarbitone, 2 benzodiazepines and 2 chloral hydrate) before blood sampling was completed.

The 37 control subjects, hospital staff and non-hospital-associated volunteers, were in good physical health and had not been exposed to any medication for at least three months. The mean age of the controls was 39.6 range 18–63 years and there were 15 male and 22 female subjects.

Psychiatric assessment

All the patients were interviewed using the Present State Examination (PSE) (Wing *et al*, 1974) within a few days of admission to hospital. In several patients, the level of disturbance was such that only behavioural items could be rated reliably; in these, the PSE was repeated when the patient was less disturbed. All depressed patients were assessed using the Hamilton Depression Rating Scale (HAMD), (Hamilton, 1960). The Brief Psychiatric Rating Scale (BPRS, Overall & Gorham, 1962) and the Modified Manic Rating Scale (MMRS, Blackburn *et al*, 1977) were introduced after the commencement of the study; the last 37 patients entered were assessed on the BPRS, and the MMRS was used for 11 out of the 16 manic patients. Six months after the patient had been discharged, the data from the PSE, the observed rating scales, and the clinical case records were assessed independently by two psychiatrists (JEC and LJW), and patients were allocated to diagnostic groups according to the RDC and the criteria of Feighner *et al* (1972). The RDC diagnosis given by each clinician was identical in 62 out of the 65 patients, and there was total agreement on the Feighner diagnosis. In three cases of disagreement, a third rater (IMB) independently reviewed the clinical data, and the diagnosis made by the 2:1 majority was accepted. Only patients with primary psychiatric disorders were included in the study; all were in good physical health, had normal plasma concentrations of urea, electrolytes and T_4, and normal liver function tests. The description of the patient population using the RDC criteria was: schizophrenia $n=24$, M/F = 20/4, mean age = 31.9 range 18–58 years; probable schizophrenia $n=2$, M/F = 1/1, mean age = 22.0 range 21–23 years; major depressive disorder psychotic sub-type $n=11$, M/F = 2/9, mean age = 47.9 range 29–59 years; major depressive disorder non-psychotic $n=4$, M/F = 3/1, mean age 46.5 range 25–72 years; minor depressive disorder $n=2$, M/F = 1/1, mean age 26.5 range 25–28 years; schizoaffective disorder depressed type $n=4$, M/F = 1/3, mean age 49.5 range 33–69 years; manic disorder $n=10$, M/F = 7/3, mean age = 35.9 range 16–71 years; schizoaffective disorder manic type $n=6$, M/F = 4/2, mean age = 39.8 range 19–54; atypical functional psychosis $n=2$, M/F = 1/1, age = 21 years in both cases.

Blood sampling

In patients and control subjects, an indwelling cannula inserted at approximately 06.40 h and left in place until 24.00 h, was kept patent by heparinised saline. Blood samples were taken at 07.00, 07.30 and 08.00 h (a.m.), 15.00, 15.30 and 16.00 h (p.m.), and 23.00, 23.30 and 24.00 h (evening). This 'neuroendocrine day' technique, designed to take account of the diurnal and pulsatile pattern of plasma cortisol concentrations, allowed calculation of mean values for a.m., p.m. and evening periods. Shortly before discharge from hospital, 28 patients agreed to and completed a repeat 'neuroendocrine day'; these were unselected, other than by being agreeable to further blood sampling. Blood samples were collected in lithium heparin-coated tubes containing 100 Kallikrein Inactivator Units Trasylol (a proteinase inhibitor added because peptide hormones were also being measured in the plasma) and kept at 4°C before and during centrifugation. Plasma was stored at −40°C until assay.

Cortisol assay

Total cortisol concentrations were determined by radioimmunoassay, using a modification of the method of Seth & Brown, (1978) with an antiserum (Scottish Antibody Production Unit) raised in sheep against cortisol −3–0–carboxy-methyloxime-bovine serum albumin. The cross-reactions of this antiserum were: cortisol, 100%; corticosterone, 0.18%; cortisone, 0.07%; 21-deoxycortisone, 0.30%; 11-deoxycorticosterone, 0.03%; 11-deoxycortisol, 0.58%; 17α-hydroxyprogesterone, 2.10%; dexamethasone, 0.33%. Anti-sheep/goat serum at a final tube dilution of 1/83 was used as the second antibody. The sensitivity of the assay (90% B/Bo) was 4.2 ng/ml cortisol. The intra-assay coefficients of variation (COV) were 2.2% (low pool; 55.3 ng/ml), 2.8% (middle pool; 112.6 ng/ml) and 3.2% (high pool; 202.8 ng/ml). The interassay COV were 4.6% (low pool), 2.68% (middle pool) and 6.34% (high pool).

Statistical analysis

The distribution of a.m. plasma cortisol concentrations in the patients and controls did not differ significantly from normal but the distributions of the p.m. and evening values were significantly skewed. The data were, therefore, log transformed to approximate normality before statistical analysis. The significance of the differences in the mean plasma cortisol concentrations between the diagnostic groups was determined by one way analysis of variance and the multiple range test of Duncan (1961). Cortisol concentrations (a.m., p.m. and evening) were correlated with age and clinical variables, using Pearson's product-moment coefficient. The paired *t*-test was used to compare plasma cortisol concentrations in the same patients when ill and on recovery.

Results

On the basis of the RDC, most of the patient population was divided into four diagnostic groups; schizophrenia ($n = 24$), major depressive disorder psychotic sub-type (MDD psychotic $n = 11$), manic disorder ($n = 10$), and schizoaffective disorder, manic type (SAM $n = 6$). The remaining 14 patients were divided into five diagnostic groups with inadequate numbers for analysis. Forty nine patients met the criteria of Feighner *et al*, (1972) for either schizophrenia ($n = 17$), depression ($n = 20$), or mania ($n = 12$), and the remainder were undiagnosed psychoses ($n = 12$).

Figure 1 shows that in the four main RDC diagnostic groups, the mean plasma cortisol concentrations were lowest in the control subjects at all three time periods. In the a.m. only schizoaffective manics had significantly greater ($P<0.05$) plasma cortisol concentrations compared with the control subjects. In the p.m., plasma concentrations of cortisol in schizoaffective manics, schizophrenics, manics and depressives were all greater ($P<0.01$ for SAM and $P<0.05$ for the other three groups) than in the control subjects. In the evening the concentration of cortisol in patients with SAM ($P<0.05$) and MDD psychotic ($P<0.05$) were greater than those in control subjects. The plasma concentrations of cortisol were higher in patients with SAM ($P<0.05$), compared with schizophrenics; this was the only significant difference between the groups of patients.

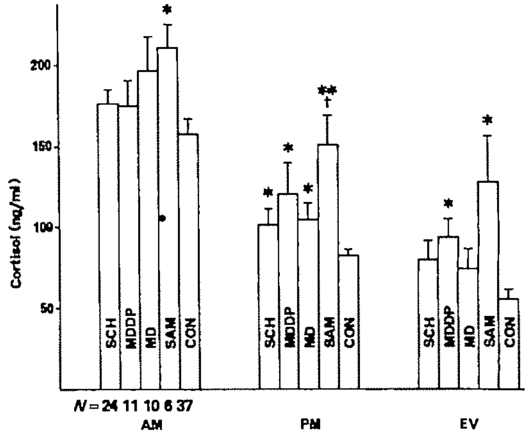

FIG. 1 Plasma cortisol concentrations (mean±SE) in patients classified according to the Research Diagnostic Criteria. Schizophrenia (SCH), Major depressive disorder psychotic subtype (MDDP), Manic disorder (MD), Schizoaffective disorder manic type (SAM), Control subjects (CON). a.m. = mean of 07.00, 07.30, 08.00 h; p.m. = mean of 15.00, 15.30, 16.00 h; ev. = mean of 23.00, 23.30, 24.00 h.
* v control subjects $P<0.05$
** v control subjects $P<0.01$
† v schizophrenia $P<0.05$

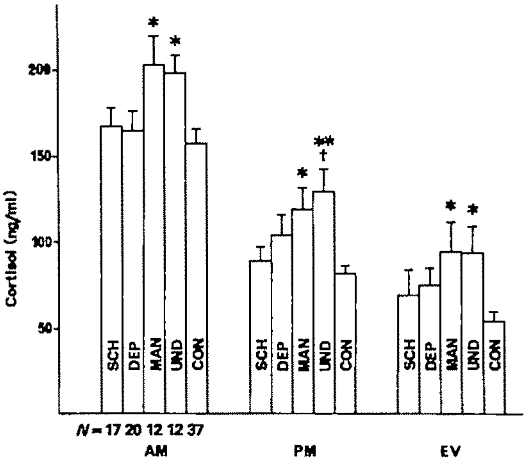

FIG. 2 Plasma cortisol concentrations (mean±SE) in patients classified according to the criteria of Feighner *et al* (1972). Schizophrenia (SCH), depression (DEP), mania (MAN), undiagnosed psychosis (UND), control subjects (CON). a.m. = mean of 07.00, 07.30, 08.00 h; p.m. = mean of 15.00, 15.30, 16.00 h; ev. = mean of 23.00, 23.30, 24.00 h.
* v control subjects $P<0.05$
** v control subjects $P<0.01$
† v schizophrenia $P<0.05$

Figure 2 shows that when classified according to the criteria of Feighner *et al*, the a.m. plasma concentrations of cortisol in patients with mania and undiagnosed psychosis were significantly greater than those in control subjects ($P<0.05$). In the p.m. the plasma concentrations of cortisol in undiagnosed psychosis ($P<0.01$) and mania ($P<0.05$) were greater than those in control subjects, and the concentrations in patients with undiagnosed psychosis were greater than those in the schizophrenics ($P<0.05$). In the evening only patients with undiagnosed psychosis ($P<0.05$) had higher plasma cortisol concentrations than those in control subjects. Patients with primary depression according to the Feighner Criteria did not have significantly higher cortisol concentrations, as compared with control subjects.

Diurnal variation

The diurnal variation of plasma cortisol concentrations was compared between the RDC groups. The cortisol concentrations were expressed as a percentage of the mean plasma cortisol concentration for the whole day, for each subject. The percentage difference between a.m. and evening percentage cortisol concentrations did not differ significantly between any of the RDC groups, nor between any RDC group and control subjects. The evening percentage of mean plasma cortisol concentration was significantly greater in depressed ($P<0.05$) compared with control subjects, but there were no other significant differences. Although there were no significant between-group differences in diurnal variation individually, many of the psychotic patients showed an unusual diurnal pattern of cortisol secretion with, in particular, increased cortisol secretion in the evening. These results will be discussed in a later publication.

Relationship between symptoms of depressed mood and plasma cortisol concentrations

There were no significant differences in the diurnal concentrations of plasma cortisol in patients with depressed mood (rated on item 23 of the PSE), compared with patients without this symptom (depressed mood $n=36$, a.m. $=174\pm9$ ng/ml, p.m. $=105\pm8$ ng/ml, evening $=$

TABLE I

Correlations between plasma cortisol concentrations and clinical variables; total score and significant items

Scale/patient group	*n*	*Plasma Cortisol Concentration ng/ml*		
		a.m.	*p.m.*	*evening*
Hamilton Rating Scale/RDC major depressive disorder and schizoaffective disorder depressed	19	−0.18	−0.38	0.23
HRS Items				
Retardation		0.29	0.24	0.48**
Loss of Insight		0.48**	0.18	0.33
Genital symptoms		0.19	−0.27	0.41*
Suicide		−0.49**	−0.35	−0.27
Psychic Anxiety		−0.39	−0.51**	−0.35
Brief Psychiatric Rating Scale/all diagnoses	37	0.01	−0.23	0.21
BPRS Items				
Grandiosity		0.31*	0.31*	0.16
Suspiciousness		0.27	0.25	0.28*
Depression		−0.23	0.31*	−0.01
Guilt		−0.20	−0.36**	−0.04
Blunted affect		−0.09	−0.42***	−0.30*
BPRS/RDC schizophrenia	13	0.48*	0.23	0.43
BPRS Items				
Grandiosity		0.26	0.46	0.54*
Emotional withdrawal		0.12	0.40	0.60**
Blunted affect		−0.50*	−0.64***	−0.31
Modified Manic Rating Scale/RDC mania and schizoaffective disorder manic type	11	−0.06	−0.18	−0.48
MMRS Items				
Has grandiose delusions		0.64**	0.48	0.06
Has persecutary delusions		0.61*	0.63*	0.34
Has poor judgement		0.52*	0.44	0.11
Is hallucinating		0.27	0.58*	0.55*
Is religiose		0.28	0.42	0.60*
Is active		−0.27	−0.54*	−0.53
Is irritable		−0.64**	−0.39	−0.21
Has diminished impulse control		−0.34	−0.60*	−0.70***
Makes threats		−0.68**	−0.48	−0.65**

*$P<0.05$
**$P<0.02$
***$P<0.01$

79±8 ng/ml; no depressed mood $n=26$, am. = 186±11 ng/ml, p.m. = 121±9 ng/ml, evening = 86±11 ng/ml). Similarly, there were no differences in plasma cortisol concentrations in those patients with and without sleep disturbance (PSE items 35 and 37) (sleep disturbance $n=49$, a.m. = 179±8 ng/ml, p.m. = 113±7 ng/ml, evening = 83±7 ng/ml; no sleep disturbance $n=14$, a.m. = 181±12 ng/ml, p.m. = 110±10 ng/ml, evening = 78±15 ng/ml). There were no significant correlations between plasma cortisol concentratons and depressed mood on the HAMD and MMRS, but on the BPRS, p.m. plasma cortisol concentrations were inversely correlated with the presence of depressed mood ($P<0.05$, Table I).

Relationship between severity of illness and plasma cortisol concentrations

In the group of patients with a depressive diagnosis (MDD psychotic, MDD non-psychotic, minor depressive disorder and schizoaffective disorder depressed type) there was no significant correlation between plasma cortisol concentrations and the severity of the depression as measured on the HAMD (Table I). The total BPRS score, irrespective of diagnosis, did not correlate significantly with plasma cortisol concentrations, but, within the RDC schizophrenic group, a.m. cortisol concentrations correlated with the BPRS score ($P<0.05$, Table I).

Relationship between HAMD, BPRS and MMRS items and plasma cortisol concentrations

Table I shows the items of the HAMD, BPRS, and MMRS which correlated significantly with plasma cortisol concentrations at one or more time points. Among this number of comparisons, by chance alone, seven significant comparisons would be expected; four at the $P<0.05$, two at $P<0.02$ and one at $P<0.01$. The observed significant correlations were 17 at $P<0.05$, ten at $P<0.02$ and three at $P<0.01$.

Effect of sedation on plasma cortisol concentrations

The patients in the RDC schizophrenia group were divided into those ($n=11$) who were entirely drug-free throughout the study period and those ($n=13$) who received a sedative drug (amylobarbitone 11 patients, phenobarbitone one patient, and chloral hydrate one patient). There were no significant differences in the plasma cortisol concentrations in patients given sedation, compared with those not given sedation (no sedation a.m. = 168±14 ng/ml, p.m. = 92±10 ng/ml, evening = 88±19 ng/ml; sedation a.m. = 183±13 ng/ml, p.m = 109±10 ng/ml, evening = 74±15 ng/ml.

Relationship between the duration of hospital stay and plasma cortisol concentrations

Figure 3 shows plasma cortisol concentrations in patients grouped according to the number of days they had been in hospital before the blood sampling. The correlation between a.m. plasma cortisol concentrations and the number of days in hospital was significant ($r=0.28$, df = 62, $P<0.05$), but neither p.m. nor evening cortisol concentrations correlated significantly with the number of days in hospital.

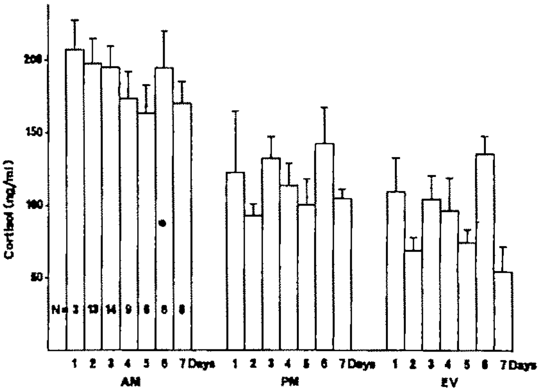

FIG. 3 Plasma cortisol concentrations (mean±SE) in patients grouped according to the number of days in hospital when the neuroendocrine day took place. a.m. = mean of 07.00, 07.30, 08.00 h; p.m. = mean of 15.00, 15.30, 16.00 h; ev. = mean of 23.00, 23.30, 24.00 h.

Plasma cortisol concentrations before discharge from hospital

The neuroendocrine day was repeated in 28 patients, shortly before their discharge. Plasma cortisol concentrations were lower before discharge, significantly in the p.m. (paired $t=2.41$, $P<0.05$) and plasma cortisol concentrations in the recovered patients were similar to cortisol concentrations in the control subjects (ill a.m. = 183±10 ng/ml, p.m. = 112±7 ng/ml, evening = 75±8 ng/ml; same patients recovered a.m. = 171±7 ng/ml, p.m. = 87±7 ng/ml, evening = 61±7 ng/ml).

Age and sex

Whilst there were considerable differences in the mean ages and sex ratios between diagnostic groups, plasma cortisol concentrations did not correlate significantly with age either in the control subjects (a.m., $r=0.00$; p.m., $r=0.15$; evening, $r=-0.05$) or within the patient groups. Cortisol concentrations were similar in the men and women in both patients and control subjects.

Discussion

The results obtained using the RDC criteria show that increased plasma concentrations of cortisol, especially during the afternoon and evening, are a feature of schizophrenia, mania, and most markedly of schizoaffective mania, as well as psychotic depression; they are therefore a feature of psychosis in general, and not specific for major depression. When the criteria of Feighner *et al* (1972) were used, only patients with mania and undiagnosed psychosis had raised plasma cortisol concentrations compared with control subjects. Patients who had an RDC diagnosis of schizophrenia, with an illness of less than six months duration, were reclassified as undiagnosed psychosis, according to the Feighner *et al* criteria. This yielded a smaller group of less acute schizophrenics, whose cortisol concentrations were similar to those of the control subjects. Feighner's criteria for primary depression allow patients with a wide range of severity to be included in a single diagnostic category. The present study sample, however, included 11 patients diagnosed by RDC as MDD psychotic, three schizoaffective disorder depressed type, two MDD endogenous sub-type, two MDD probable endogenous sub-type and only two minor depressive disorder. Thus, raised plasma cortisol concentrations were associated with depressive psychosis, and the inclusion of patients without psychotic symptoms but meeting the Feighner *et al* criteria for primary depression, yielded a mixed group of depressed patients whose plasma cortisol concentrations did not differ significantly from those of controls.

As might be expected from previous studies, the morning plasma cortisol concentrations were the least useful in discriminating psychotic patients from control subjects. The greatest differences in plasma cortisol concentrations between patients and controls were seen in the afternoon, but there was still considerable overlap, except in the case of the schizoaffective manics.

Depressed mood is common in psychoses, but comparison of patients from all diagnostic categories with and without depressed mood did not reveal an association between increased plasma cortisol concentrations and depression. Furthermore, increased plasma cortisol concentrations were not associated with the presence of depressed mood, as rated on the BPRS, HAMD, or MMRS. High plasma cortisol concentrations appear, therefore, to be a feature of acute psychoses and not of depression. Clinical variables associated with raised plasma cortisol concentrations were: retardation, loss of insight, and (less consistently) loss of libido on the HAMD in depressed patients; grandiosity and emotional withdrawal on the BPRS in schizophrenics; the presence of grandiose and persecutory delusions, loss of judgement, hallucinations, and religiosity on the MMRS in manics; and across diagnoses, grandiosity and suspiciousness on the BPRS. Thus, raised plasma cortisol concentrations appear to be primarily associated with psychotic features such as loss of insight or paranoia. The severity of illness, as measured by the total score on the HAMD, BPRS, or MMRS, was not related to plasma cortisol concentrations. All these rating scales, however, contain a number of items relating to non-specific neurotic symptoms such as anxiety, some of which are negatively correlated with high plasma cortisol concentrations. In a cross-diagnostic study of morning and evening plasma cortisol concentrations, Swigar *et al* (1979) reported that evening concentrations were higher in patients with more severe types of illness (primary affective, schizophrenic and schizoaffective) as compared with milder illness (reactive depression, situational reactions, neuroses, and behavioural and personality disorder). Their findings are in agreement, therefore, with the results of the present study in suggesting that it is particularly those patients with psychotic symptomatology who have raised plasma cortisol concentrations in the evening.

Raised plasma cortisol concentrations in psychotic patients cannot be attributed to the stress of hospital admission because the cortisol concentrations were similarly raised whichever day a patient was sampled, during the first week in hospital. Nor can raised plasma cortisol concentrations be attributed to the acute effects of amylobarbitone. Gamma-aminobutyric acid has an inhibitory effect on the secretion of ACTH (Elias *et al*, 1982) and it would, therefore, be expected that acute administration of amylobarbitone would decrease ACTH release and thus plasma cortisol concentrations. Furthermore, despite the inevitable fact that the more disturbed patients were given sedation, within the schizophrenic group there were no significant differences in plasma cortisol concentrations between those patients who had or had not sedation. On recovery from any type of psychotic illness, plasma cortisol concentrations returned to levels close to those in control subjects irrespective of whether the patient was treated with antidepressants, neuroleptics, lithium, or ECT. This finding is in agreement with previous studies in depressed patients (Carroll *et al*, 1976; Christie *et al*, 1982), providing strong evidence for the view that raised plasma cortisol concentrations in psychotic patients are dependent upon the illness, and that lowering of the plasma cortisol concentration is dependent upon recovery from illness rather than upon the nature of the treatment.

Although the present study shows that raised plasma cortisol concentrations are a feature of psychotic patients, irrespective of diagnosis, this does not mean that the increase in cortisol concentrations is a non-specific response to stress. On the contrary, it is the clinical symptoms specific to psychosis, paranoid and grandiose delusions, hallucinations, and loss of insight which correlate positively with raised plasma cortisol concentrations and not non-specific symptoms such as psychic and somatic anxiety and agitation. This suggests that psychotic patients have an abnormality in the control of the hypothalamic-pituitary-adrenocortical system and that this abnormality may be related to the pathogenesis of psychotic symptomatology.

There are several possible neurochemical interpretations of increased plasma cortisol concentrations. At the peripheral level, increased cortisol concentrations may reflect a direct effect of circulating catecholamines acting through β_2 adrenoreceptors in the pituitary to increase the release of ACTH (Mezey *et al*, 1983). Increased urinary excretion of adrenaline, noradrenaline, and their metabolities have been reported in patients with depression and mania (Schildkraut *et al*, 1978; Koslov *et al*, 1983). Jimerson *et al*, (1983) have reported a positive correlation between urinary MHPG in depressed patients and pre- and post-dexamethasone cortisol concentrations, and a preliminary study by Barnes *et al*, (1983) reported higher plasma adrenaline and noradrenaline concentrations in dexamethasone non-suppressors. In a large population of depressed patients Stokes *et al*, (1984b) have shown an association between increased function of the hypothalamic-pituitary-adrenocortical system and the urinary excretion of adrenaline. The central neuronal control of corticotrophin releasing factor (CRF) is complex, with involvement of many neurotransmitters including noradrenaline, acetylcholine, 5-hydroxytryptamine, γ-aminobutyric acid, opiates, and vasopressin (Weiner & Ganong, 1978; Buckingham, 1980; Rivier & Vale, 1983). The understanding of the neuronal control of CRF release, while limited in the rat, is considerably more uncertain in the human. The use of a variety of pharmacological challenges has provided some evidence to support the hypothesis that a central noradrenergic deficit underlies the hypercortisolaemia of depressed patients. For example, the initial elevation of plasma cortisol concentrations induced by amphetamine is blunted in depressed patients (Checkley & Crammer, 1977; Sachar *et al*, 1980; Feinberg *et al*, 1981); the high baseline morning cortisol concentrations of depressed patients are subsequently reduced by dextroamphetamine, so that 90 minutes after the drug, they have similar cortisol concentrations to control subjects (Sachar *et al*, 1980); the α_2 agonist clonidine reduces plasma cortisol concentrations to a greater extent in depressed patients, as compared with control subjects (Siever *et al*, 1984).

Thus, the results of the present study show that raised plasma cortisol concentrations, particularly in the afternoon and evening, are a feature of drug-free patients with an acute psychotic illness irrespective of diagnosis. Raised plasma cortisol concentrations are not a specific feature of patients with severe depression, and are not related to the presence of depressed mood, but are associated with the presence of psychotic symptoms.

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*Janice E. Christie, MPhil, MRCPsych, *Clinical Scientist, Honorary Consultant.*

Lawrence J. Whalley, MD, MRCPsych, *Clinical Scientist, Honorary Consultant.*

Heinz Dick, M.I.S.T., *Technician.*

Douglas M. R. Blackwood, PhD, MRCPsych, *Clinical Scientists, Honorary Senior Registrar.*

Ivy M. Blackburn, PhD, *Clinical Scientist, Top Grade Psychologist.*

George Fink, MD, DPhil, *Director.*

MRC Brain Metabolism Unit, Royal Edinburgh Hospital, Morningside Park, Edinburgh EH10 5HF.

*Correspondence

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Dexamethasone Concentrations and the Dexamethasone Suppression Test in Psychiatric Disorders

HOWARD MORRIS, VAUGHAN CARR, JUDY GILLILAND and MICHAEL HOOPER

The dexamethasone suppression test (DST) has been widely used in psychiatry as a laboratory aid for the diagnosis of endogenous depression; failure to suppress serum cortisol levels is interpreted as confirming a clinical diagnosis of endogenous depression. We found that serum dexamethasone concentrations in this test vary widely and are determinants of the DST response: non-suppression of serum cortisol levels is associated with low serum dexamethasone concentrations, and suppression is associated with high concentrations.

Considerable psychiatric research in recent years has involved the application of neuro-endocrine strategies for investigating the biological aspects of psychiatric disorders. In particular, Carroll *et al* (1981) developed a laboratory test for melancholia (endogenous depression), the 1 mg overnight dexamethasone suppression test (DST), which depends on the suppression of plasma cortisol levels following an oral dose of dexamethasone. Subsequently, the DST became widely employed in both clinical practice and in psychiatric research. It had been originally reported that the test had a diagnostic specificity for in-patients of 96% with a sensitivity of 67%, using a plasma cortisol criterion of 138 nmol/l (5 μg/dl). However, recent research suggests that these figures, especially for specificity, may be inflated, in comparison with those derived from broad clinical populations. For instance, failure to suppress serum cortisol levels after 1 mg of dexamethasone has been reported in a substantial proportion of patients with acute psychosis, schizophrenia, alcoholism, panic disorder, dementia, and other psychiatric disorders, as well as in some normal subjects (Amsterdam *et al*, 1982; Raskind *et al*, 1982; Swartz & Dunner, 1982; Balldin *et al*, 1983; Coppen *et al*, 1983; Gwirtsman *et al*, 1983; Hällström *et al*, 1983; Sheehan *et al*, 1983; Targum, 1983; Targum & Capodanno, 1983).

The dose of dexamethasone used was reported to have a major effect on the sensitivity of the DST (Carroll *et al*, 1981), indicating indirectly that the suppressibility of plasma cortisol in patients with endogenous depression was dependent on the plasma dexamethasone concentration. An earlier study of plasma dexamethasone levels in the DST reported no difference in the elimination half-life of dexamethasone in patients with endogenous or non-endogenous depression respectively (Carroll *et al*, 1980). No significant correlation between plasma cortisol and dexamethasone concentrations was found when test results from cortisol suppressors and non-suppressors were analysed together. A more recent report (Meikle, 1982) on the plasma dexamethasone levels found a six-fold variation in the plasma concentration following a 1 mg oral dexamethasone dose in normal subjects.

In the present study, we determined simultaneous serum concentrations of cortisol and dexamethasone in the course of the DST, in a series of psychiatric patients, to establish if there was any relationship between serum dexamethasone concentrations and the DST response.

Method

The subjects for this study ($n = 66$) were drawn from a consecutive series of admissions to an adult psychiatric unit in a general teaching hospital; this is not a research unit, and patients represented a cross-section of all psychiatric disorders. On admission, height and weight were recorded, and the DST performed within 72 hours. Diagnoses were made by consensus between two qualified psychiatrists, using DSM-III (American Psychiatric Association, 1980) criteria, and were based on clinical interview and case records. Each patient was interviewed jointly and the psychiatrists were blind to the DST results.

The DST protocol was that described by Carroll *et al* (1981) and involved serum cortisol estimations at 0800, 1600, and 2300 hours after the ingestion of 1 mg of dexamethasone at 2300 hours the previous day. Serum cortisol concentrations were determined by radioimmunoassay (Amerlex, Amersham International, Amersham, UK), with a coefficient of variation (interassay) of 10% at 160 nmol/l (5.8 μg/dl). The criterion for non-suppression following a DST was failure to suppress the serum cortisol concentration below 160 nmol/l (5.8 μg/dl) in any one of the three samples. Using this DST procedure and cortisol assay, 94% of normal volunteers ($n = 35$) with no history of psychiatric illness were found to suppress their serum cortisol concentrations below the criterion value (Boyce *et al*, 1983).

Serum dexamethasone was assayed by radioimmunoassay, using highly specific antisera, ^{3}H-dexamethasone (Amersham International, UK) and a dextran-charcoal separation procedure. The antibody was prepared in rabbits against the dexamethasone C-3 carboxymethyloxime protein antigen. The cross-reactivity with cortisol was less than 0.02% and the dexamethasone assay was unaffected by serum cortisol concentrations up to 1300 nmol/l (52 μg/dl). Consequently, a preliminary chromatography step was not necessary before radioimmunoassay. The sensitivity of the assay was 0.2 nmol/l (8 ng/dl) and imprecision of the assay was 8% (coefficient of variation) at 5 nmol/l (180 μg/dl).

Results

Within the total group of patients tested, 39 were found to be non-suppressors and 27 suppressors, following dexamethasone; 15 met the medical exclusion criteria specified by Carroll *et al* (1981) and, therefore, data from these patients were not included in the following analyses. There were 18 patients with major depressive disorder, 10 (56%) of whom were DST non-suppressors and 32 patients with other psychiatric diagnoses, 15 (46%) were DST non-suppressors. The diagnoses of patients without major depressive disorder included schizophrenia (6), adjustment disorder (6), personality disorder (4), dysthymic disorder (4), psychogenic pain disorder (2), schizo-affective disorder (2), bipolar disorder, depressed (2), bipolar disorder, manic (1) and one each of the following: alcohol dependence, primary degenerative dementia, schizophreniform disorder, atypical anxiety disorder, generalised anxiety disorder and panic disorder.

Mean serum cortisol and dexamethasone concentrations at each time of sampling for the non-suppressors and suppressors are presented in Table I. The mean serum cortisol levels for the non-suppressor group were significantly higher at each time than those of the suppressor group, but were not significantly different from normal controls. Conversely, the mean serum dexamethasone levels at each time were significantly lower for the non-suppressor group, when compared with the suppressor group.

TABLE I

Serum Cortisol and dexamethasone concentrations

Serum Cortisol (nmol/l)							
Time	*Non-suppressors*			*Suppressors*			
(Hours)	n	$\bar{X}$	SEM	n	$\bar{X}$	SEM	*P*
0800	24	350	47	26	67	6	<0.001
1600	25	379	34	26	50	4	<0.001
2300	25	209	26	26	46	4	<0.001
Serum Dexamethasone (nmol/l)							
Time	*Non-suppressors*			*Suppressors*			
(Hours)	n	$\bar{X}$	SEM	n	$\bar{X}$	SEM	*P*
0800	24	5.30	0.65	26	10.10	0.73	<0.001
1600	25	1.35	0.30	26	2.51	0.27	<0.01
2300	25	0.37	0.11	26	0.77	0.13	<0.025

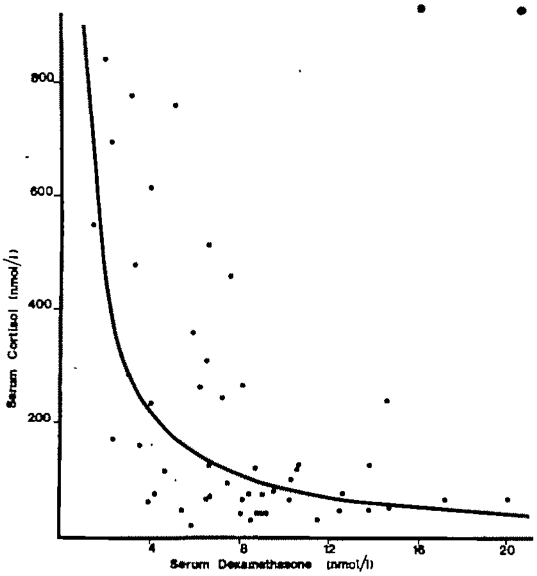

FIG. 1 Correlation of serum cortisol and dexamethasone concentrations from 50 patients at 0800 hours. The line describes the equation (Cortisol) = 852 (Dexamethasone)$^{-1}$. The distribution of the data points about the line was highly significant ($r = 0.59$, $P < 0.001$; $F = 25.4$, $P < 0.001$).

The simultaneous serum cortisol and dexamethasone concentrations at 0800 hours are presented in Figure 1. The equation

$$(\text{Cortisol}) = 852\ (\text{Dexamethasone})^{-1}$$

describes a highly significant inverse relationship between them, ($n = 50$, $r = 0.59$, $P < 0.001$; $F = 25.4$, $P < 0.001$). A linear relationship between these parameters was not expected. This is because cortisol and dexamethasone differ in their biological activity.

At 1600 hours, this inverse relationship was maintained and described by the equation: (Cortisol) = 136 (Dexamethasone)$^{-0.34}$ ($n = 51$, $r = 0.32$, $P < 0.05$).

The relationship was not significant at 2300 hours, possibly because most of the serum dexamethasone concentrations were below the level of sensitivity of the assay (<0.2 nmol/l).

The elimination half-life of serum dexamethasone was calculated for each patient and the mean times for the non-suppressor (3.4±0.30 hours ($\bar{X}$±SEM)) and suppressor groups (3.9±0.25 hours) were not significantly different ($P > 0.05$). No significant relationship was found between serum dexamethasone levels achieved and body weight, surface area, or body mass index (weight/height^2). Similarly, no significant relationship was found between DST response and age or sex of the patients included in this study. Urinary dexamethasone/creatinine ratios in samples collected between 2300 hr. day 1 (time of oral dexamethasone dose) to 0800 hr. day 2 (time of first serum sample) in non-suppressor patients were significantly lower than suppressor patients ($P<0.01$).

Discussion

These results demonstrate significant individual variation of the serum dexamethasone concentration, following a 1 mg oral dose, and the dexamethasone level was strongly associated with the DST response. They confirm an earlier study in which a very similar distribution of serum dexamethasone levels was found in normal subjects at 0800 hours, following a 1 mg oral dexamethasone dose (Meikle, 1982), but are at variance with the findings of Carroll *et al* (1980), who reported only a 'minor' variation of plasma concentrations with psychiatric patients. Few radioimmunoassays for dexamethasone determinations have been reported, though the assays of Meikle (1982) and Carroll *et al* (1980) were similar, in that both incorporated a preliminary chromatography step. Because of the increased specificity of the antibody used in the present study, this step was not required. The range of serum dexamethasone concentrations following an oral 1 mg dose reported here is identical to that found by Meikle, indicating that there was no interference by cortisol in this assay.

The serum dexamethasone levels were significantly inversely related to the serum cortisol concentrations. The patients with the lower dexamethasone concentrations tended to be those with the higher serum cortisol concentrations, and were non-suppressors on the DST. On the other hand, patients with the higher serum dexamethasone concentrations tended to have lower serum cortisol concentrations, and were DST suppressors. The data indicate that the serum dexamethasone level contributes significantly to the result of the DST. There was no difference between the serum dexamethasone concentrations of the non-suppressor patients with major depressive disorder and of those with other psychiatric disorders. The considerable overlap of the serum dexamethasone concentrations between the non-suppressor and suppressor groups, in both diagnostic categories, indicates that some patients achieved substantial dexamethasone levels, but still failed to suppress their cortisol concentration, presumably because of increased activity of the hypothalamic-pituitary-adrenal axis. There is no evidence from our data, however, that this was more prevalent in patients with major depressive disorder than in those with other psychiatric diagnoses.

Our data do not rule out the possibility that the variation in the serum levels is due to variable absorption of dexamethasone from the gastrointestinal tract. There was no significant difference between the rate of elimination of dexamethasone by the non-suppressor group with low serum levels and the suppressor group with higher serum dexamethasone levels. Preliminary data on urinary dexamethasone levels indicate an increased concentration in the suppressor group, when compared with the non-suppressor group. This suggests that the renal excretion of dexamethasone is dependent on the serum concentration and is not contributing to the variation in serum levels between the two groups. The volume of distribution does not appear to make a significant contribution to the variation of the serum levels, as there was no correlation of serum dexamethasone concentration with body weight, surface area, or body mass index which correlates strongly with obesity (Garrow, 1980; Lee *et al*, 1981; Knapp, 1983).

The conclusions based on these findings are twofold. Firstly, it cannot be assumed that a fixed oral dose of dexamethasone produces a constant serum dexamethasone level, so that it may be suitable to modify the test procedure, using parenteral administration of dexamethasone. Secondly, in the oral 1 mg overnight DST, the wide variability of serum dexamethasone concentrations is a significant determinant of the DST response. Whilst this manuscript was in preparation, it was brought to our attention that a number of groups have reported a similar association between DST non-suppression and low serum dexamethasone concentrations (Holsboer *et al*, 1984; Johnson & Hunt, 1984; Krieg *et al*, 1984. Thus, until the relationship between serum dexamethasone and cortisol concentrations is further clarified, interpretation of DST results should be made with due caution. As currently performed, the usefulness of the DST as an aid for the diagnosis of endogenous depression in clinical practice should be reconsidered.

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*Howard Morris, BSc, PhD, *Principal Hospital Scientist, Division of Clinical Chemistry, Institute of Medical and Veterinary Science, Adelaide, South Australia, 5000.*

Vaughan Carr, MB, BS, FRCP(C), FRANZCP, *Lecturer in Psychiatry, University of Adelaide, Adelaide, South Australia, 5000.*

Judy Gilliland, BSc, *Senior Hospital Scientist, Institute of Medical and Veterinary Science, Adelaide, South Australia, 5000.*

Michael Hooper, MB, BS, FRACP, *Clinical Endocrinologist, Royal Adelaide Hospital, Adelaide, South Australia, 5000.*

*Correspondence

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Depression, Urinary Free Cortisol Excretion and Lymphocyte Function

ZIAD KRONFOL, J. DANIEL HOUSE, JOSEPH SILVA JR., JOHN GREDEN and BERNARD J. CARROLL

An impairment in lymphocyte response to mitogen stimulation, a correlate of cell-mediated immunity, has been reported in patients with depressive illness. To investigate whether such impairment in lymphocyte function is related to excessive secretion of cortisol, an immunosuppressive hormone, we compared mitogen-induced lymphocyte proliferation in three groups of subjects: (1) depressed patients with elevated 24-hour urinary free cortisol (UFC) excretion; (2) depressed patients with normal UFC excretion; and (3) normal controls. Depressed patients in both groups showed significant reductions in lymphocyte mitogenic activity, in comparison with the normal controls, but the two depressive groups did not significantly differ from each other in their lymphocytic responses to any of the mitogens used. Furthermore, no significant correlations were found, within depressed patients, between UFC excretion and lymphocyte mitogenic responses. Depression is therefore associated with an impairment in lymphocyte function that cannot be explained solely on the basis of increased cortisol secretion.

The immune system is closely associated with both the central nervous system and the endocrine system (Rogers *et al*, 1979; Riley, 1981); recent developments in the psychobiology of the affective disorders suggest an increase in hypothalamic-pituitary-adrenal (HPA) activity in some but not all patients with depression (Carroll, 1982). This is usually manifested by increases in cortisol levels in plasma, CSF, and urine of depressed patients, compared to normal controls (Carroll *et al*, 1976a, 1976b). Other HPA abnormalities in depression include a disruption of the circadian pattern of cortisol secretion (Sachar *et al*, 1973) and plasma cortisol resistance to suppression by dexamethasone (Carroll, 1982). Physiologically, this increase in HPA activity in depression may result in a state of hypercortisolaemia, of varying intensity and duration. Since one major effect of hypercortisolaemia is suppression of immune function (Dougherty *et al*, 1964; Claman, 1972), and since impaired immunity has been observed in depressed patients (Kronfol *et al*, 1983; Schleifer *et al*, 1984), we postulated that depressed patients with hypercortisolaemia will have lower immunological competence than depressed patients without this. To test this hypothesis, we compared immune function in depressed patients with and without hypercortisolaemia and normal controls. The immunological parameter studied was lymphocyte response to mitogen stimulation—a correlate of cell-mediated immunity (Oppenheim *et al*, 1975). HPA activity was assessed with measures of 24-hour urine free cortisol, which is a sensitive indicator of adrenocortical function (Beardwell *et al*, 1968; Tyler & West, 1972) and a good index of circulating unbound and physiologically active plasma cortisol levels over time (Burke & Beardwell, 1973; Carroll *et al*, 1976c). We found that depressed patients had lower lymphocytic responses than normal controls, but that this lowering of immunological competence in depression was not related to increased levels of UFC excretion.

Method

Subjects

Three groups of subjects were identified: (1) depressed patients with hypercortisolaemia ($n = 11$); (2) depressed patients without hypercortisolaemia ($n = 22$); and (3) normal controls ($n = 20$). Hypercortisolaemia was defined, on the basis of UFC excretion, as levels exceeding 100 μg/24 hours; this was based on published reports on UFC determinations using similar techniques and showing mean UFC values for the normal population in the range of 33–48 μg/24 hours, with less than 5% of the normal population having values in excess of 100 μg/24 hrs (Murphy, 1968; Beardwell *et al*, 1968; Hsu & Bledsoe, 1970). The 100 μg/24 hours criterion has also been used by our group to differentiate between depressed and non-depressed psychiatric patients (Carroll *et al* 1976b; Carroll *et al*, 1976c).

All patients were evaluated at the Clinical Studies Unit of the Department of Psychiatry, University of Michigan Medical Center; they all met the Research Diagnostic Criteria (Spitzer *et al*, 1977) for major depressive disorder. Controls were healthy volunteers with no history of psychiatric illness. Demographic features of the three study groups are presented in Table I. Depressed patients with elevated UFC tended to be older than the other two groups, but these differences were not statistically significant (F = 1.83; df = 2,50; NS). Similarly, there were no significant differences in the sex distribution of the three groups ($X^2 = 0.83$; df = 2; NS). Severity of depression, as reflected by scores on the Hamilton Depression Rating Scale (HDRS—Hamilton, 1960), was not significantly different between the two depressive groups (t = 1.9; df = 31, NS). All patients and controls were in good physical health and were drug-free for at least two weeks prior to the immune evaluation. Informed consent was obtained from all participants.

TABLE I
Demographic features

Diagnosis (n)	Age	Sex (M:F)	HDRS
Depression with elevated UFC (11)	48.8±18.1	4:7	19.7±5.5
Depression with normal UFC (22)	42.0±18.2	7:15	15.3±6.3
Normal Controls (20)	36.7±14.9	8:12	—
P values	NS	NS	NS

Procedure

1. UFC. Urine collections for 24-hour UFC determinations were started on Day 1 at 2300 hours and completed on Day 2 at 2300 hours. Urine volumes were recorded and UFC levels measured using a modified version of the competitive protein-binding assay (Murphy, 1968; Carroll, 1976b). Mean urinary volume in the depressed patients with hypercortisolaemia was 1287±651 ml. Mean UFC value in these patients was 147.0±34.4 μg/24 hour. Mean urine volume in depressed patients without hypercortisolaemia was 1086±598 ml. Mean UFC was 60.3±20.3 μg/24 hours. The difference in urine volume between these two groups was not statistically significant (t = 0.88; df = 31; NS). The difference in 24-hour UFC was highly significant (t = 9.13; df = 31; $P < .0001$).

2. Lymphocyte response to mitogen stimulation. Twenty milliliters of blood were collected from each subject at 0800 hour on Day 2 of the study; all samples were thus drawn during the same 24-hour period of the urine collection. The blood was centrifuged over Ficoll-Hypaque and the lymphocytes separated and washed; lymphocytes were then re-suspended in a culture medium (Kronfol *et al*, 1983). Triplicate lymphocyte cultures were established in microtiter plates. To each well were added 10^5 lymphocytes from the culture medium and one of the following mitogens: Phytohemagglutinin-P (PHA), 25 μg/ml, Concanavalin A (Con A), 10 μg/ml or Pokeweed Mitogen (PWM), 1:10 dilution. These doses of mitogen were used because they were associated with optimal stimulation in dose-response curves obtained earlier in our laboratory. Lymphocytes from all subjects were also cultured without mitogen for background stimulation. All cultures were incubated at 37°C for 96 hours—a culture period determined in our laboratory to provide optimal results; at this point, 1 μCi of tritiated thymidine was added to each well, and six hours later, the cultures were harvested on to glassfibre filter paper, washed, and air-dried. Tritiated thymidine uptake, indicative of the mitotic activity of the lymphocytes, was measured with a scintillation counter. The arithmetic means of the triplicate samples for each subject were then calculated. The lymphocyte response to each mitogen was expressed as the difference in scintillation counts per minute (cpm), between mitogen and background counts.

3. Statistical analysis. The arithmetic mean (±SD) of the lymphocyte response to each mitogen in each group was calculated and recorded. For statistical comparisons between the groups we used the student t test. For correlations between the endocrine and immune variables, we calculated Pearson's correlation coefficient r. All levels of significance were two-tailed.

Results

The background (unstimulated) counts for the three study groups were as follows: 346±176 cpm for depressed patients with elevated UFC; 835±480 cpm for depressed patients with normal UFC and 558±288 cpm for normal controls. The lymphocytic responses to the mitogens PHA, Con A, and PWM in the three groups were calculated as described above and illustrated in Figure 1. Depressed patients with elevated UFC had significantly lower lymphocytic responses to the mitogens PHA (t = 3.43; df = 29; p = .0018), Con A (t = 2.45; df = 29; $P = .0207$) and PWM (t = 3.27; df = 29; $P = .0028$) than the normal control group. Depressed patients with normal UFC also had significant reductions in their lymphocytic responses to PHA (t = 2.66; df = 40; $P = .0113$), Con A

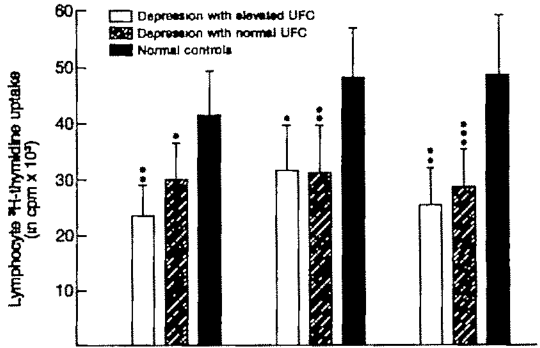

FIG. 1 Lymphocyte response to mitogen stimulation in depressed patients with and without hypercortisolaemia and normal controls. Comparisons are made between each of the depressed group and the normal controls.

*$P < .05$ **$P < .01$ ***$P < .001$

(t = 3.18; df = 40; $P = .0028$) and PWM (t = 3.62; df = 40; $P = .0008$) when compared to the normal controls. However, when depressed patients with elevated UFC were compared to depressed patients with normal UFC, no significant differences emerged. Lymphocyte responses to PHA (t = 1.42; df = 31; NS), Con A (t = 0.10; df = 30; NS) and PWM (t = 0.67; df = 31; NS) were not significantly different in these two groups.

We then examined the relation between UFC and lymphocyte function for the entire depressed group (*n* = 33). Table II shows the results of correlations between 24-hour UFC values and lymphocytic responses to the three different mitogens. There were no significant associations between UFC and lymphocytic responses to any of the mitogens used.

TABLE II

Correlations between UFC and lymphocyte response to mitogen stimulation in all depressed patients

Mitogen	*Pearson's r*	*n*	*P*	*Significance*
Phytohemagglutinin-P	−.22	33	.23	NS
Concanavalin A	+.0009	33	.99	NS
Pokeweed mitogen	−.06	33	.69	NS

Discussion

We have earlier reported a suppression of mitogen-induced lymphocyte proliferation in patients with depressive illness (Kronfol *et al*, 1982; Kronfol *et al*, 1983; Kronfol & House, 1984). These findings have also been replicated by independent investigators (Schleifer *et al*, 1984). However, none of the studies published so far has compared lymphocyte function in neuroendocrine sub-types of depression and normal controls. Our data indicate that depressed patients, regardless of cortisol secretion, have lower *in-vitro* lymphocyte mitogenic responses than normal controls. Lymphocyte response to mitogen stimulation is known to be affected by a number of factors such as age, diurnal variation, medical illness, and drugs. There were no significant differences in the age or sex distribution of our depressed patients and normal controls. All subjects were free of drugs or medical illness known to interfere with lymphocyte proliferation *in-vitro*. All blood samples were collected at the same time of the day to minimize possible effects of diurnal variation. Severe malnutrition has also been associated with immunosuppression, but our depressed patients were not malnourished (mean weight: 66.4 kgs). It is possible that the stress of hospitalisation may affect immune function, but since most of our patients had been in the hospital for a two-week drug washout period prior to immune testing, the stress of acute hospitalisation was unlikely to have played a major role.

Our findings also indicate, rather surprisingly, similar lymphocytic responses in depressed patients, regardless of the presence of hypercortisolaemia. Since elevated cortisol levels are usually associated with immunosuppression (Claman, 1972; Britton *et al*, 1975), we had expected depressed patients with elevated UFC to have lower lymphocytic responses than depressed patients with normal UFC, but our data did not support this hypothesis. We also failed to establish any significant correlation among depressed patients between UFC excretion and lymphocytic responses. Although it is not clear at what level of cortisol the lymphocyte function becomes disturbed, it is possible that the hypercortisolaemia observed in our depressed patients may not be severe enough to affect the immune response (Fauci, 1978). It is also possible that depression with hypercortisolaemia is associated with a state of glucocorticoid resistance which minimizes the physiological effects of cortisol (Schlecte & Sherman, 1985). Alternatively, it is possible that the immunosuppression in depressed patients may not be related to cortisol, but to other hormones or neurotransmitters which have been postulated to play a role in the pathophysiology of depression, such as catecholamines, serotonin, acetylcholine, and endorphins (Van Praag, 1982). Since all of these substances have also been shown to regulate the immune response (Hall & Goldstein, 1981), it is possible that a derangement in the metabolism of one or more of these substances in depression may be responsible for the observed immunological aberrations in depressed patients (Kronfol, 1985; Kronfol & Schlechte, 1985).

Thus, diminished parameters of immune function have been observed in patients with depressive illness. The present data indicate that this suppression of immunological competence is not related to an increase in levels of cortisol, an immunosuppressive hormone. We are presently studying the relationship between lymphocyte function and other biological and clinical variables in depressive illness. Further research is needed into the 'psychoneuro-immunology' of the affective disorders and into the relationship betwen hormones, mood, and the immune response in depressed patients to clarify some of these complex issues.

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*Ziad Kronfol, MD, *Assistant Professor, Department of Psychiatry, University of Iowa College of Medicine, Iowa City, Iowa 52242. USA.*

J. Daniel House, PhD, *Assistant Research Scientist, Department of Family Practice, University of Iowa.*

Joseph Silva Jr, MD, *Professor of Internal Medicine (Infectious Diseases), University of Michigan Medical Center, Ann Arbor, Michigan 48109.*

John Greden, MD, *Professor of Psychiatry, University of Michigan.*

Bernard J. Carroll, MD, PhD, *Professor and Chairman, Department of Psychiatry, Duke University School of Medicine, Durham, North Carolina, 27710.*

*Correspondence

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Hormones, Mood and Sexuality in Lactating Women

E. M. ALDER, A. COOK, D. DAVIDSON, C. WEST and J. BANCROFT

Of 25 primiparous women, investigated prospectively for six months post-partum, 19 persisted with breast feeding and six changed to artificial during the first six weeks. Sexual activity, mood, and feeding patterns were recorded in weekly diaries. Hormones were measured from weekly urine samples (oestrogen and pregnanediol) and fortnightly blood samples (prolactin, testosterone, androstenedione, and sex hormone binding globulin). In breast-feeding women, testosterone and androstenedione levels were significantly lower in those who reported severe reduction in sexual interest. Changes in sexuality or mood were not related to levels of prolactin or oestrogen, or to the return of follicular activity, which was delayed in persistent breast feeders. The relationships of mood, sexuality, and hormones are discussed.

The post-partum period is one of major change; apart from the impact of the new child, the mother has to adjust to her altered physical state. Depression occurs in 12 to 15% (Kumar & Robson, 1978; Cox *et al*, 1982), and there is an increased likelihood of admission to psychiatric hospitals (Kendell *et al*, 1976, 1981). Sexual activity declines during pregnancy, taking some time to return to its pre-pregnancy level (Robson *et al*, 1981), and clinical experience suggests that sexual problems commonly start during the post-partum period (Bancroft, 1983).

Of the various factors that could affect mood and sexuality during this period, the hormonal status of the woman has often been considered (Brockington & Kumar, 1982). There is an invariable and massive change in hormonal status following birth, once the placenta is delivered. Attempts to relate hormonal changes to the mood changes that commonly occur within the first few days of delivery have so far been unsuccessful (Nott *et al*, 1976), though recent studies of platelet monoamine activity (Metz *et al*, 1983) and plasma amines (Kuevi *et al*, 1983) offer more hope of doing so. As far as later effects during the puerperium are concerned, the main determinant of the hormonal state is the pattern of feeding. Lactating women have high prolactin levels, which depend in part on the suckling frequency of the baby, and whilst prolactin is raised, ovarian activity is usually suppressed, with consequently low levels of oestrogen and progesterone (Howie *et al*, 1981). By contrast, the artificial feeding mother has usually returned to normal ovarian cyclicity between six and 15 weeks after delivery (Glasier *et al*, 1983; Howie *et al*, 1982).

Little attention has been paid to lactation in recent studies of post-partum behavioural change, and when it has been considered, this has usually been very superficially, e.g. by categorising women as having breast fed or not, without taking into account the duration of breast feeding and whether supplementary feeds have been added. Yet without such information, no adequate conclusions can be drawn about their hormonal status.

Aims of study

This was a prospective investigation of the sexuality and mood of lactating women, using self-report diary data as well as interview ratings, to relate behavioural changes to hormonal changes over a six-month post-partum period.

Method

Subjects

Thirty-nine consecutive attenders at two ante-natal clinics in the Simpson Memorial Maternity Pavilion who were primiparous, at 30 weeks gestation, married, living in Edinburgh, English speaking, and intending to breast feed, were asked to participate after having the study fully explained to them. Twenty-seven (72%) agreed, 12 refusing on the grounds of dislike of venepuncture (7), reluctance to record sexual activity (3) or lack of interest (2). Those who subsequently used artificial feeding methods continued in the study unless they also used combined oral contraceptives—one woman was excluded on these grounds—and one other was withdrawn because her baby was critically ill. This left 25 women who completed their participation in the study. Their mean age was 26.1 years (range 20-38, S.D. = 3.8) and mean length of marriage was 4.3 years (range 0–9, S.D. = 2.1). Five were from social class I, nine from II, nine from III and two from IV.

Interview

All subjects were interviewed at 36 weeks ante-natally and at 12 and 24 weeks postnatally. The ante-natal interview covered social background, attitude to and previous knowledge of breast feeding, self-ratings of health, and sexual and marital relationships. At the post-natal interviews, mothers were asked about breast feeding, health, and sexual and marital relationships. Only those interview items reported here will be described.

Frequency of sexual intercourse during the three months preceding conception and during each trimester of pregnancy was established by direct questioning, as was occurrence and frequency of orgasm during sexual activity before and during pregnancy. At each post-natal interview the woman was asked to compare her interest or appetite for sex with pre-pregnancy levels, and was rated as experiencing 'more', 'no change in' or 'less' sexual interest. Those reporting less were then asked further detailed questions, and were rated by the interviewer as either having 'severe' loss of interest (i.e. sufficient to be regarded by the woman as a problem) or not.

Mood was assessed by the response to the questions "During the past three months, have you felt miserable or down?" and "During the past three months, have you felt especially well or happy?". Both answers were self-rated as "not at all", "a little", or "a lot". Those reporting being miserable were asked whether they had sought medical help or received treatment.

Diaries

Each woman completed a weekly diary form throughout the 24 post-partum weeks of the study (Alder & Bancroft, 1983). This recorded frequency of feeds and also sexual behaviour (i.e. sexual intercourse, sexual contact with partner not involving coitus, masturbation, and orgasm). Frequency of sexual thoughts and associated feelings of sexual excitement were rated for the previous week, using two visual analogue scales. Mood during the previous week was measured on ten visual analogue scales for the following characteristics: motherly, cheerful, sociable, energetic, confident, tense, irritable, fatigued, depressed, and changeable (Sanders *et al*, 1983).

Hormones

Each woman was visited fortnightly throughout the 24-week post-partum period for blood sampling (and collecting diaries). Ten millilitres of venous blood were taken at least two hours after the previous breast feed, to avoid the transient changes following suckling. Plasma was separated and stored at −20°C until assayed with specific radioimmunoassays for prolactin (McNeilly & Hagen, 1974), testosterone (Corker & Davidson, 1978) and androstenedione (Baird *et al*, 1974), both androgens after chromatography. Sex hormone binding globulin (SHGB) was assayed as described by Anderson *et al* (1976).

Early morning urine samples were collected once weekly and assayed for total oestrogens and pregnanediol. Hormone concentrations were expressed in terms of the hormone creatinine ratio as described in Glasier *et al* (1983).

Analysis of Results

To assess the relationship between sexuality or mood and hormonal status, two methods were used.

1. Mean levels of urinary oestrogens and pregnanediol and median levels of plasma prolactin, testosterone, and androstenedione for weeks 4 to 20 were correlated with mean measures of sexuality and with four measures of mood (cheerful, sociable, fatigued, and depressed) for the same time period.
2. Points in time when changes in hormone levels occurred—the first sign of follicular development, and the first ovulation were identified in each woman and behavioural measures were compared before and after these time points. Follicular activity was defined as a rise of more than ten micrograms total oestrogen per 24 hours, and ovulation as a rise in oestrogens plus a rise in pregnanediol greater than 1 mg/24 hrs (Howie *et al*, 1982; Howie & McNeilly 1982).

Results

Behaviour post-partum

Infant feeding

Six women changed to artificial feeding before six weeks and will hereafter be referred to as the artificial feeders. Further details of feeding patterns have been reported elsewhere (Alder & Bancroft, 1983).

Contraception

All of the artificial feeders used non-steroidal methods of contraception. Five of the breast feeding women used a progestogen-only oral contraceptive (Noriday). The remainder used non-steroidal methods.

Sexual activity

The mean interval between delivery and the first occasion of sexual intercourse was 6.7 weeks (S.D. = 3.8, range 2–16); 50% had had intercourse by six weeks post-partum and 88% by twelve weeks. For 12 to 24 weeks, the mean weekly frequency was 1.2 occasions weekly ($n = 25$), compared with a recalled pre-pregnancy frequency of 2.6 occasions weekly ($P < 0.01$). Sexual contact not leading to coitus was reported by 18 women on at least one occasion, with the highest frequency in the first few weeks before sexual intercourse had been resumed. The mean interval between birth and such contact was 2.7 weeks (S.D. = 0.92, range 2–5) (Alder & Bancroft, 1983). There was a longer delay before orgasm returned: whereas all 25 women had been orgasmic before pregnancy, only 19 had experienced orgasm during the study period. The mean interval between delivery and first orgasm was 6.9 weeks (S.D. = 4.6, range 2–18), but the proportion of occasions of intercourse associated with orgasm rose during the first six weeks of resumed sexual activity.

Four women (16%) masturbated during the six-month period. For one woman, a breast feeder, this was her principal form of sexual activity; for another, it was no more frequent than intercourse, largely occurring when her husband was away on shift work. The other two masturbated only occasionally.

There was a tendency for the artificial feeders to resume sexual intercourse earlier and with higher frequency than the breast feeders (see Alder & Bancroft, 1983). Self-ratings of frequency of sexual thoughts and associated feelings of excitement increased with time, but with no significant difference between the artificial and breast feeding groups.

Interview ratings of sexual interest at 12 weeks showed that 14 (74%) of the breast feeding mothers experienced a reduction in sexual interest, which persisted until 24 weeks in 11 (53%). In five (26%), this loss was rated as 'severe'. This contrasts with only two out of the six of the artificial feeders reporting reduction in sexual interest, which neither rated as severe. No women reported an increase of sexual interest, compared with pre-pregnancy levels.

Mood changes

None of the women had had previous treatment for depression. At interview, 76% of women reported feeling especially well or happy during pregnancy and 83% during the first three months of post-partum. However, 72% had felt miserable or down (a little or a lot) at some stage during pregnancy, and 66% during the first three months post-partum. Two women (one breast and one artificial feeder) were treated for post-natal depression.

On the visual analogue mood scales, the majority of women rated themselves highly on positive items and low on negative items. Apart from some increase in the ratings of positive items over the first six weeks, there was no consistent change over the six-month study period. There were no differences in mood ratings between artificial and breast feeders.

Hormone changes post-partum

All of the six artificial feeders had shown follicular activity, and all had ovulated, by 15 weeks. In contrast, only three of the breast feeding mothers (15%) had shown evidence of follicular activity by 16 weeks and only nine (47%) by 24 weeks. Only two breast feeders had shown evidence of ovulation by the end of the study.

Prolactin

Prolactin levels dropped rapidly after delivery in the artificial feeders, from a mean of 943 mu/L (S.D. = 571) at four weeks to a mean of 181 mu/L (S.D. = 36) at 22 weeks. Within the breast feeding group, high levels (mean at four weeks 1499 mu/L, S.D. = 1190) were maintained for a longer period, followed by a gradual decline to a mean of 649 mu/L (S.D. = 463) at 22 weeks, which was only partially attributable to the suckling frequency. Five of the 19 breast feeders had prolactin levels within the non-pregnant range (i.e. less than 500 mu/L) by 12 weeks, though they did not differ from the other breast feeders in frequency of breast feeding.

Androgens

Testosterone, androstenedione, and SHBG levels did not show any consistent pattern of change during the 24 weeks, though there was considerable individual variation in levels. The medians of the eight samples taken between weeks 4 and 20 were calculated. Androstenedione median levels were significantly higher in artificial feeders than in breast feeders (1747 ng/ml and 1150 ng/ml; $P = < 0.05$, Mann Whitney two-tailed test) and lower in breast feeding women taking the progestagen-only pill compared with those not using steroidal contraception (800 ng/ml and 1306.5 ng/ml; $P = < 0.02$). Testosterone showed the same pattern. (Artificial feeders 608.5 ng/ml, breast feeders, 355 ng/ml, $P = < 0.002$); pill-using breast feeders 301 ng/ml, non-pill breast feeders, 399 ng/ml $P = < 0.02$). SHBG levels showed the same trends, though significance was only at the 10% level (artificial feeders 143.8 nMol/L, breast feeders 53.3 nMol/L; pill-using breast feeders 51.8 nMol/L, non-pill breast feeders 57.2 nMol/L).

Relationship between hormones and behaviour: (1) sexuality

Oestrogens and Pregnanediol

The 14 breast feeders not using oral contraceptives had mean levels of total oestrogens and pregnanediol for weeks 4–20 ranging from 2.1 to 5.9 mgm/ml oestrogens and from 0.17 to 0.6 mu/l pregnanediol. There was a significant correlation between the pregnanediol level and frequency of sexual thoughts ($rs = 0.65$, $P < 0.05$), but none of the measures of sexuality correlated with oestrogen levels.

In the 11 breast feeding women who showed a return to follicular activity, there was no difference in measures of sexuality before and after the oestrogen rise. These women with reduced sexual interest assessed at interview did not differ from the rest in their levels of pregnanediol or oestrogen.

Prolactin

Medians of the prolactin levels in the eight samples collected between weeks 4 and 20 ranged from 580 to 1525 mU/L. These levels did not correlate with any measure of sexual behaviour, and women with reduced sexual interest did not have significantly different levels of prolactin.

Androgens

Medians of androgen levels in the eight samples collected between weeks 4 and 20 ranged from 660 to 2341 pg/ml androstenedione, 206 to 682 pg/ml testosterone and 23.1 to 105.3 nMol/l SHBG. Correlations between these levels and ratings of sexual activity or sexual thoughts were not significant. However, women with severely reduced sexual interest, assessed at interview, had significantly lower levels of both androstenedione and testosterone (Table I).

This pattern was consistent over time, as shown in Figs. 1 and 2. SHBG levels showed no association with any measure of sexual behaviour.

Relationship between hormones and behaviour: (2) mood

In the fourteen breast feeders who were not using oral contraceptives, there were no significant correlations between mood and oestrogen or prolactin levels.

Both androstenedione and testosterone were significantly correlated with ratings of 'sociable' (rs = +.73, $P<0.05$ and rs = .71, $P<0.05$ respectively) and with ratings of 'cheerful' (rs = +.46, $P<0.1$ and rs = +.56, $P<0.1$). The testosterone was negatively correlated with 'fatigue', rs = −.63, $P<0.05$. SHBG levels did not correlate with any of the mood scales.

TABLE I

Median androstenedione and testosterone levels and sexual interest over six months post-partum in 14 breast feeders not using oral contraceptives

Rating at three months interview	*n*	Medians Androstenedione µg/ml	 Testosterone pg/ml
Reduced sex interest	5	1034	355
No reduced sex interest	9	1530	464
(Mann Whitney, one-tailed)		P<0.01	P<0.01

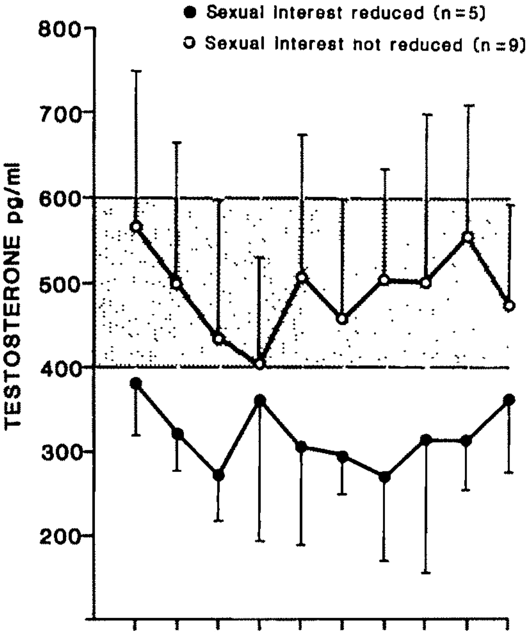

FIG. 1 Levels (means and s.d.) of testosterone in 14 breast feeders (non-pill). The shaded area represents the range in normal women (mean 501, S.D. 100, Sanders 1981). Analysis of variance: F = 6.72, d.f. 1, 12; $P<0.05$.

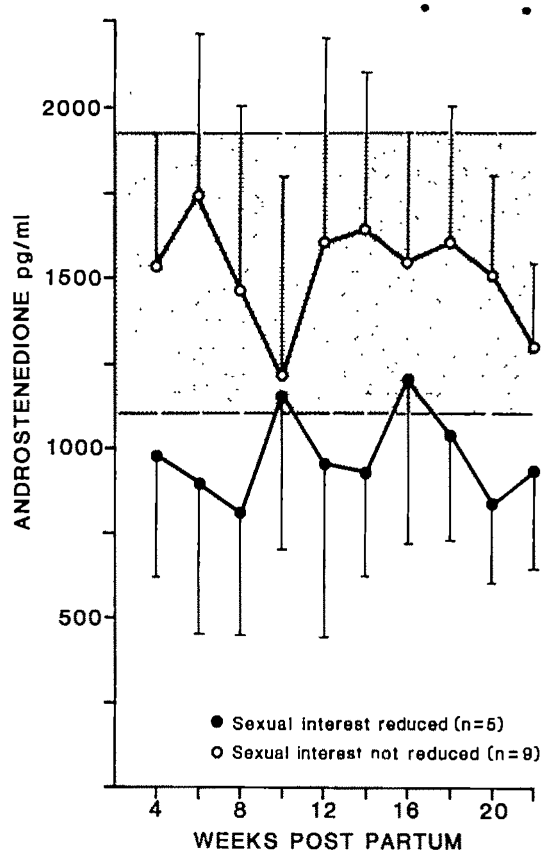

FIG. 2 Levels (mean and s.d.) of androstenedione in 14 breast feeders (non-pill). The shaded area represents the range in normal women (mean 1540, S.D. 377, Sanders 1981). Analysis of variance: F = 6.12, d.f. 1, 12; $P<0.05$.

Discussion

The reduction in frequency of sexual activity during the post-partum period in this study is comparable to that reported in previous studies (Robson *et al*, 1981; Baxter, 1974; Falicov, 1973), but evidence of changes in sexual interest in the post-partum has been less often reported. Our results suggest the possibility that women who are breast feeding are more likely to experience loss of sexual interest than those using artificial feeds, though further research is required to establish whether this is the case. In none of our women was there any evidence that breast feeding enhanced sexuality, as was reported by Masters & Johnson (1966).

Two women (8%) were treated for depression, one by her GP and one as a psychiatric out-patient;

this incidence is not much less than would be expected (Kumar & Robson, 1978). In this small group, there were no differences in mood ratings between those fully and those partially breast feeding, although Alder & Cox (1983) reported a higher incidence of depressive symptoms during the first three months in non-pill taking women who fully breast fed.

The only striking relationship between hormones and behaviour that emerged involved androgens. There is very little previous evidence about androgen levels during the post-partum period in either breast feeding or artificially feeding women. Due to the fact that a substantial proportion of androgen comes from the ovary, the suppression of follicular development that is typical in the early stages of lactation would be expected to result in lower androgen levels. Our findings that the breast feeding women had lower testosterone and androstenedione levels than the artificial feeders therefore comes as no surprise, but the further suppression associated with the progestogen-only pill requires explanation. This may be due to preferential binding by progestogen, displacing androgens (Victor *et al*, 1976), though that would be more relevant to testosterone than androstenedione, which is bound to a much smaller extent.

Of particular interest is the association between the androgen levels and the loss of sexual interest. The role of androgens, testosterone in particular, in female sexuality is proving to be complex compared with their role in men, and much of the evidence is apparently conflicting. We have suggested elsewhere various explanations for this complexity: long-term developmental effects of androgen on personality in women may sometimes conflict with conventional heterosexuality (Sanders & Bancroft, 1982), and women may vary in their genetic sensitivity to hormonal effects on behaviour (Bancroft, 1984). In this prospective study, we have identified hormone-behaviour relationships which are presumably of very recent onset. It is conceivable that if we had assessed these women some months later, and assuming that their loss of sexual interest had persisted, the hormone-behaviour relationship might have become obscured by the confounding effects of psychological and interpersonal processes.

This interesting and potentially important observation has to be qualified, however. The number of women involved is small, and we cannot exclude the possibility that the difference in androgen levels preceded the difference in sexual interest. The observed association was with the interview ratings of loss of sexual interest. Correlations with self-ratings of sexual thoughts, whilst positive, were not significant. In men, similar self-ratings have reflected androgen effects (Skakkebaek *et al*, 1981; Wu *et al*, 1982; O'Carroll & Bancroft, 1984). It may be that self-reported frequency of sexual thoughts is a more relevant indicator of sexual appetite in men than in women, and that direct questions about sexual interest or appetite are more meaningful to women. This methodological issue deserves further scrutiny. Also, in view of the significant correlations we observed between androgens and certain aspects of mood, notably 'sociable', 'cheerful' and 'fatigued', it is possible that the sexual effect was part of a non-specific effect. Mood and sexuality are probably not independent (Sanders *et al*, 1983).

High levels of prolactin in men predictably impair sexual interest (Bancroft *et al*, 1984). Evidence from hyperprolactinaemic women is more limited, but there is some evidence of adverse effects on sexuality (Buvat *et al*, 1978) and mood (George *et al*, 1980). During lactation in the early months, prolactin levels are significantly higher than in normal non-pregnant women, and there are further bursts of prolactin following nutritional suckling, which may reach very high levels.

We have excluded the transient peaks of prolactin from our data by the timing of blood samples, and this may account for our negative findings. Further studies of hyperprolactinaemia and sexuality and mood in women are certainly required.

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E. M. Alder, BSC, PhD, *Senior Research Officer.*

A. Cook, SRN, SCM, *Research Sister.*

D. Davidson, HNC, AIMST, *Technical Research Assistant (Higher).*

C. West, MB, ChB, MRCOG, *Senior Registrar, Ward 36, Royal Infirmary of Edinburgh, Lauriston Place, Edinburgh EH3 9YW.*

*J. Bancroft, MD, MRCP, FRCPsych, *Clinical Consultant.*

MRC Reproductive Biology Unit, Centre for Reproduction Biology, 37 Chalmers Street, Edinburgh EH3 9EW.

*Correspondence

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Computed Tomography in the Elderly:
Changes over Time in a Normal Population

JONATHAN M. BIRD, RAYMOND LEVY and ROBIN J. JACOBY

The clinical, psychometric, and computed tomographic (CT) status of previously fit elderly volunteers is described at follow-up for up to four years. A number of relationships were found between psychometric and CT scores, but a dementing group could not be determined on the basis of a single scan. However, a subtle reduction in cognition over time was significantly related to CT changes, and occurred in 10%. Larger ventricles were also found in a small sub-group, who developed late-onset depressive disorders; recent bereavement was related to ventricular size. Thus a single CT scan may not be a useful discriminatory test in early dementia, but a repeat demonstrating ventricular enlargement, is likely to be significant. In the elderly, cognitive and CT scan deterioration should not be expected unless a disease process is occurring; this may be indicated by subtle cognitive impairment or by late-onset depressive disorder.

The computed tomographic (CT) brain scan is a harmless, non-invasive procedure, offering the possibility of following changes in the radiological presentation of the brain over time with ease and considerable safety. It is surprising, therefore, that few long-term follow-up studies of either psychiatric patients or controls have been carried out. Ron (1983) commented that her study of alcoholics appeared to be the largest follow-up to date; Naguib & Levy (1982a,b) followed a group of dementing patients and were able to re-scan ten patients.

We are not aware of any previous CT follow-up studies of fit elderly people, which is perhaps in part due to the technical difficulties of assessing scan changes over time. Du Boulay *et al* (1978) pointed out that differences of head positioning between scans constitute the major technical problem, which is only partly solved with the use of expensive equipment and a considerable increase in radiation dose. Other technical problems (Bird, 1982) cause a variation of up to 20% in measures taken from the same scanning machine. However, in a large group, there is no reason to suppose that technical factors would lead to error in any particular direction. Individual errors should cancel each other out, or their effects may be taken into account, using partial correlation techniques.

To understand the significance of CT changes over time in elderly patients, it would seem necessary to know whether the scan normally changes in the fit elderly population. The significance of "atrophy" (ventricular dilatation or sulcal widening) is unclear, and there is considerable overlap between patients with dementia and controls (Jacoby & Levy, 1980a). The scan appears to be an important prognostic indicator of mortality both in depression in the elderly (Jacoby *et al*, 1981) and in dementia (Naguib & Levy, 1982a), but the importance of CT appearances in the prognosis of the fit elderly population is not clear.

In this paper, we report the cognitive status and CT scan appearance at follow-up of a group of initially healthy elderly people, assessed after a period of up to four years. Our intention has been, firstly, to gather further data in an area which has not been widely investigated to date, and secondly, to test a number of hypotheses concerning changes in clinical and CT status as well as the relationships of these changes over time.

Method

Subjects

These consisted of 50 volunteers over the age of 60, who formed the basis of an earlier CT study (Jacoby *et al*, 1980). All had been carefully screened then to ensure the absence of detectable psychiatric and neurological disorder.

Initial clinical data

For the earlier study, a psychiatric and neurological history was obtained, general personal data collected, and brief mental state and neurological examinations performed. In addition, the Mental Test Score (Hodkinson, 1973)—a test of memory and orientation—was administered.

Follow-up clinical data

All subjects were successfully traced. At two years, three had died, and before testing could be completed, altogether five had died. All subjects (45) still alive were seen; one refused to be interviewed fully. The mean follow-up period was 136 weeks (range 62–200 weeks); 27 subjects agreed to undergo a repeat CT scan, on the same scanner as was originally used (EMI CT 1010).

At follow-up, we carried out: (1) history update (marital status, physical or psychiatric illness, medication, recent bereavement or life change); (2) psychiatric examination; (3) the Mental Test Score (MTS—Hodkinson, 1973); (4) the Parieto-Temporal Score (PTS—Jacoby & Levy, 1980a); (5) the Digit Copying Test (DCT—Kendrick, 1984); (6) The Digit Symbol Substitution sub-test of the WAIS (DST—Wechsler, 1955); (7) the Paired Associate Learning Test (PALT—Inglis, 1959); and (8) the Benton Visual Retention Test (Benton, 1973—both the score of correct results, BVRTS, and of errors, BVRTE).

The psychometric tests were chosen to assess a wide range of cognitive abilities, including general orientation and memory (MTS), parieto-temporal functioning (PTS), speed at copying (DCT), symbol substitution (DST), new verbal learning (PALT) and new visual learning (BVRT).

Radiological data

The original scans (Jacoby *et al*, 1980) were reassessed for ventricular size by planimetric Ventricular Brain Ratio (VBR) measurement and for measurement of the Anterior Horn Index (AHI)—(Haug, 1977); this is also called the Evans Ratio (Evans, 1942). The neuroradiologist's original ratings of cortical atrophy and ventricular size were also used.

All of these measures were also taken for the 26 repeat CT scans, and an analysis of regional brain density was carried out on the original and follow-up scans. The method used for regional brain density measurement was described by Bondareff *et al* (1981) and by Naguib & Levy (1982a). To control for any variations in regional brain density measurements due to the date of scanning, partial correlation techniques were used.

Results

Catamnestic and clinical data

Mean age at follow-up was 76 (range 64–92): 23% aged 70–79, and 14% aged 80 and over; 10% had died over a three-year period. When the 27 survivors who agreed to have a repeat CT scan were compared with the 18 who refused, the only significant difference was that the refusers had a larger original planimetric VBR ($P = .029$). All other catamnestic data, original and current cognitive data and original CT data showed no significant differences.

Of those still alive, 24 had remained physically well, 13 had had a new physical illness and were treated at home, and 13 had been admitted to a hospital. None had suffered a severe intracranial disorder, 6% had been prescribed psychotropic medication, and one referred to a psychiatrist for depression. Sixteen were not receiving any medication at the time of follow-up. Of the remainder, one was receiving an antidepressant and 16 wesre receiving night sedation. Six subjects had suffered the loss of a spouse within the previous year.

Cognitive and psychological data

The means and standard deviations for these are presented in Table I.

TABLE I
Scores on psychometric tests at follow-up

	Mean	*S.D.*	*Range*
Mental test score at initial testing	32.1	(1.7)	(28–34)
Mental test score at follow-up	31.9	(2.2)	(25–34)
"Parieto-temporal score"	1.9	(2.1)	(0–9)
Digit copying test	90.0	(26.4)	(27–145)
Digit symbol substitution test	29.2	(10.7)	(4–55)
Paired associate learning test	22.9	(17.6)	(1–64)
Benton visual retention test (score)	4.4	(2.2)	(0–8)
Benton visual retention test (errors)	9.4	(3.9)	(3–18)

Intercorrelation between cognitive scores

Significant correlations at the 1% level were found between MTS and all cognitive measures except PALT ($P<0.001$ in the case of DCT, DST, and BVRTS). All other cognitive scores related significantly ($P<0.01$) with each other, again except for PALT. The correlation between PALT and other results did not reach the 1% significance in any case, and only in the cases of PTS and BVRTS did it reach a significance of 5%. The total PTS was made up of six sub-scores; of these, copying a series of asymmetrical drawings correlated in a highly significant fashion ($P<0.001$) with the other psychological test scores except PALT. Other sub-scores did not perform as well.

Relationship of cognitive data to CT data at follow-up

Mental test score. At follow-up, MTS related in a significant inverse fashion ($r = -.54$ and $-.48$, $P<0.01$) to ventricular size (VBR and AHI). It also related to thalamic brain densities on both sides ($r = .37$ and $.45$, $P<0.01$) and to frontal and occipital brain densities on both sides ($P<0.05$). In these calculations, age was controlled for, using partial correlation techniques.

It was also found, on assessing the previous scans, that the initial MTS correlated with occipital brain densities ($P<0.05$), although, as previously reported (Jacoby *et al*, 1980), it did not correlate with ventricular size.

Other cognitive tests: Further significant correlations ($P<0.05$) were found at follow-up between the Digit Copying Test and right frontal density; between the Digit Symbol Substitution Test and cortical atrophy score; between the Paired Associate Learning Test and both occipital brain densities; between the Benton Visual Retention Test (BVRT) score and VBR, AHI, and left occipital brain density; and between BVRT errors and VBR, cortical atrophy score and left parietal brain density.

Atrophy versus no atrophy—using CT score cut-off points: The data were also examined by dividing cases into those falling on the dementing side of the CT scan cut-off points defined in Jacoby & Levy (1980a) and those falling on the normal side. Cut-off points were as follows: cortical atrophy score of 4, ventricles rated normal or large, VBR of 17 or AHI of 34. There were no significant cognitive differences between the two groups, divided for each CT parameter in this way, using two-tailed t-tests.

Changes in cognitive and CT scores

In the group as a whole, no significant overall changes were seen in MTS, nor in any of the CT scores (including brain density scores), over the period of follow-up. This seems a resilient and stable group of elderly people.

However, in those subjects who showed a drop in MTS score over the follow-up period, there was a highly significant associated increase in ventricular size, both VBR ($r=-.40$, $P=0.002$) and AHI ($r=-.40$, $P=0.002$). A reduction in MTS of more than three points was found to be associated with a number of follow-up cognitive test results and initial and follow-up CT measures (Table II). This occurred in five subjects (10%).

TABLE II
Significant associations with a reduction in Mental Test Score (MTS)

	Associated cognitive tests at follow-up	*Associated CT measures*
MTS reduction of >3 points over follow-up period	Low digit symbol substitution test score ($P<0.05$) Low Benton visual retention test score ($P<0.05$)	Higher follow-up VBR ($P<0.001$) Greater increase in VBR ($P<0.05$) Lower left thalamic brain density at follow-up ($P<0.05$)

(Significance refers to two-tailed t-test)

Using the cut-off points suggested in Jacoby & Levy (1980a) the group was divided into two subgroups for each initial CT score. Differences in follow-up cognitive scores were assessed using two-tailed t-tests; these cut-off points did not predict any differences in cognitive scores at follow-up.

Multiple regression analyses were carried out in an attempt to build up a predictive model of cognitive abilities at follow-up, based on initial CT scores. The coefficient of determination (r^2) values obtained from the multiple regression programme of SPSS indicate what proportion of the variation of a dependent variable can be explained by the independent variable. This figure is therefore quoted here as an indicator of how successful a predictor of future cognition any individual CT score may be.

Initial CT scores had between 13% and 30% success in predicting variation in future cognitive scores in most cases. This is poor. However, variations in DCT, DST, and PALT were all predicted at a level of more than 50% when brain density scores were included as independent variables. Variation in BVRTE was predicted (52%) by inclusion of initial ventricular and cortical atrophy ratings only. In general, brain density scores were better as predictors of follow-up cognitive scores than were the ventricular and cortical atrophy ratings.

Recent bereavement

The only life-change which related significantly to CT data was the recent death of a spouse; this occurred in six subjects (12%). Bereavement significantly correlated with both measures of ventricular size at follow-up, even when controlling for age (VBR—partial correlation coefficient .35, $P<0.04$, AHI—partial correlation coefficient .45, $P<0.01$). Bereavement did not correlate significantly with initial ventricular size.

Changes in health

Onset of physical illness during follow-up period (occurring in 53%) was related to greater initial AHI ($P<0.05$). Psychiatric disorder between testing had occurred in four cases and consisted entirely of depressive illness (according to hospital and GP notes). Depressive disorder was associated with larger ventricles on initial CT scan (VBR—$P<0.001$, AHI—$P<0.05$, neuroradiologist's assessment—$P<0.001$) and follow-up CT scan (VBR—$P<0.05$), but not with cognitive scores. Only one individual remained significantly depressed at the time of interview.

Discussion

We believe this to be the first report of the rescanning of a group of fit elderly people. It was hoped that this would give some insight into the normal and pathological changes occurring over time in a larger group of elderly people, some of whom were previously fit (Jacoby *et al*, 1980), some previously depressed (Jacoby & Levy, 1980a; Jacoby *et al*, 1981; Jacoby *et al*, 1983) and some suffering from dementia (Jacoby & Levy, 1980b; Naguib & Levy, 1982a,b). It should be noted that members of each of the three groups (normal, depressed, demented) were chosen so as to make the groups clearly demarcated, so that changes occurring in subjects who are initially at the borderlines of these conditions are not being studied. It does, however, mean that if subjects do cross the borders, their associated changes may have a more clear-cut significance. This study refers only to subjects over the age of 60.

Cognition and CT scan at one time-point

There is general agreement that marked atrophy on CT scan is significantly associated with clinical dementia (Huckman *et al*, 1975; Fox *et al*, 1975; Synek & Reuben, 1976; Synek *et al*, 1976; Jacoby & Levy, 1980a). There is, however, considerable overlap; up to 20% of normal elderly people have ventricles which are larger than expected for their age, and 25% of dements have ventricles which are within the normal range (Jacoby & Levy, 1980a). Some disagreement exists, since Earnest *et al* (1979) found that atrophy and mental impairment are merely accompaniments of normal ageing.

In the present study, results of a general orientation and memory test were found to be related to ventricular size and to frontal, thalamic and occipital brain densities, while a variety of other cognitive scores were related to CT measurements. This scattering of relationships between tests and CT scores might be taken to indicate that many are chance findings, and larger numbers are needed to confirm them. However, it may suggest that tests of supposedly localised functions are in fact assessing a variety of complex abilities—as perhaps indicated by the relationship between a test of new verbal learning (PALT) and both occipital brain densities. There is some debate about whether brain densities are of clinical significance (Naeser *et al*, 1980; Bondareff *et al*, 1981; Naguib & Levy, 1982a,b; Wilson *et al*, 1982), but in this study, the variety and number of significant correlations between brain densities and clinical scores suggest that there are important relationships.

Thus, it appears that even in an apparently fit elderly person, a CT scan taken at one point in time may bear a significant relationship to cognitive abilities. However, it is important not to place undue significance on cut-off points of dementia; it is now clear that those determined in our earlier studies cannot be used in an elderly population to define a dementing group, and that the CT scan forms only part of the investigation of a case of possible dementia. Atrophy does not necessarily indicate dementia; the diagnosis must still be made by means of a global clinical assessment. As our follow-up results demonstrate, it is only over the course of time that a relationship between cognitive condition and CT scores may become clarified.

Changes in cognition and CT scores over time

In the present, initially fit group, the results of a test of memory and orientation (MTS) remained remarkably stable over the follow-up period, as did all the CT scores for the group as a whole. However, a small sub-group (10%) emerged, in whom a reduction in MTS was associated with low scores at follow-up on some other cognitive tests, with larger ventricles and lower left thalamic brain densities, and with an increase in ventricular size over the follow-up period.

These results would seem to indicate that a reduction in scores on a simple test of memory and orientation over a period of two to four years is an important finding, and is likely to be associated with evidence of structural brain changes. This figure of 10% fits well with the expected prevalence of dementing disorders in the elderly in the community (Kay *et al*, 1964), but further follow-up would be required to assess whether this sub-group progressed to a true dementing picture.

In the original study of this group, Jacoby *et al* (1980) commented on the reciprocal relationship between cortical atrophy and memory and orientation score, suggesting that this might be evidence either of a non-progressive impairment—the benign senescent forgetfulness of Kral (1962)—or the beginnings of senile dementia. At follow-up, those designated as having more cortical atrophy were now found to have significantly larger ventricles, but did not differ from the rest on any of the cognitive tests. Contary to Kral's view, this would seem to indicate that whilst some sort of brain degeneration may progress, the cognitive abilities do not necessarily deteriorate. Indeed, the process should perhaps rather be termed benign senescent atrophy. Our data support the view that ventricular enlargement is a better indication of cognitive impairment than is cortical atrophy.

Inter-correlations of cognitive scores

It is interesting that all the cognitive scores, except the PALT, correlated well with each other. This would seem to suggest that MTS, DCT, DST and BVRT were all measuring a similar group of variables, while the PALT assessed some different skill or ability. We observed that a poor result on the PALT might be produced more by a lack of comprehension of the instructions than by memory impairment, whereas in the other four tests used here, the instructions to the subject were very simple. A further factor was that in the other four tests, mistakes were not usually obvious to the subject, whilst in the PALT, he was made aware of his mistakes and corrected accordingly, leading at times to increased embarrassment and to loss of concentration.

Prediction of cognition from CT scan

The finding that future cognitive impairment could not be predicted by using initial CT cut-off scores further underlines the need for caution in the use of such measures. In particular, it demonstrates that in the elderly, a single finding of large ventricles may not be an indication of a dementing process. If, however, ventricles are enlarging over time (even if they are still not excessively large), then this may well be a pointer to some organic brain disease. This confirms results found in clearly dementing patients who were re-scanned (Brinkman & Largen, 1984). Predictive attempts, using multiple regression analysis, demonstrated that variation in future cognitive abilities is determined largely by factors other than those which can be measured on a CT scan. However, in a few tests (DCT, DST, PALT), it was found that initial brain density measurements, when added together, could predict more than half of the variation in future cognitive scores. In general, brain density measurements had much greater predictive value than ventricular or cortical atrophy scores.

Changes in health and life circumstances

Almost 9% of subjects had apparently suffered a first episode of depressive illness but the criteria for admission to the study excluded any person with a previous history of depression. This depressive group had significantly larger ventricles, both initially and at follow-up, but did not have abnormalities on psychometric testing. Thus, this small group of late-onset depressives with larger ventricles would seem to bear out a number of our previous findings, including the existence of a sub-group of late-onset depressives with larger ventricles who, at follow-up, appeared to have a higher mortality rate than those with normal ventricles. We also found that ventricular enlargement was not apparently associated with a worse clinical course of depression. In the present sub-group of late onset depressives, the clinical course did not seem to be severe, since three out of the four had fully recovered at follow-up, and only one required hospitalisation. Late-onset depression was also not associated with markedly decreased cognitive abilities at follow-up. It is of interest that the ventricular enlargement appears to predate the onset of depression, which would further confirm the hypothesis, suggested by Post (1968) and by ourselves, that an ageing process facilitates the emergence of depression in late life and that ventricular enlargement is another, apparently earlier, manifestation of this. A larger prospective study would further elucidate these findings and it will be important to carry out further follow-up studies of this group.

A relationship was also found between bereavement and ventricular size at follow-up (but not initially). This is difficult to explain, and the sub-group of bereaved were not the same subjects as the sub-group of depressives. Since the recently bereaved suffer an increased mortality (Parkes *et al*, 1969), ventricular enlargement may be part of some general process in this group, but a larger study would be needed to confirm this finding.

Our results suggest two main conclusions. The first is that evidence of atrophy on a single CT scan need not indicate present or future dementia. The second is that, in a group of initially fit elderly people, there is no reason to expect a deterioration in cognitive abilities or CT scan results, unless some disease process is occurring. Our results suggest that such a disease process may be indicated by fairly subtle cognitive deterioration or by the late onset of a depressive illness, both of which seem to be associated with ventricular enlargement. Taken together, these clinical and CT changes indicate a pathological process, and are not part of normal ageing.

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Jonathan M. Bird, BSc, MB, ChB, MRCPsych, *Senior Registrar*

Raymond Levy, PhD, FRCP(Ed), FRCPsych, *Professor of the Psychiatry of Old Age*

Robin J. Jacoby, DM, MRCP, MRCPsych, *Consultant Psychiatrist*

The Bethlem Royal and Maudsley Hospitals and the Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF, England

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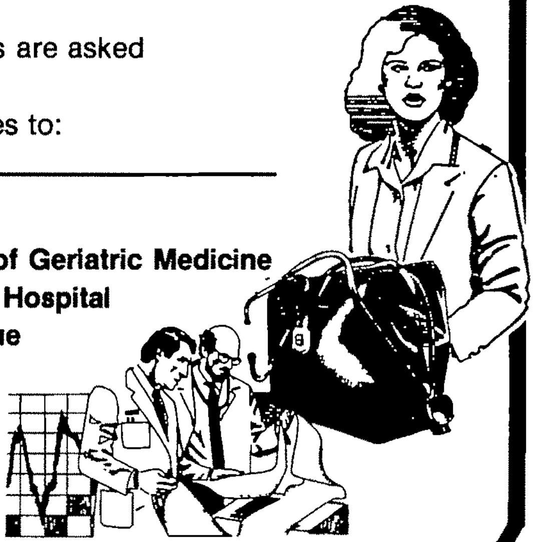

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Pseudodementia: Facts and Figures

A. BULBENA and G. E. BERRIOS

The historical and conceptual aspects of the pseudodementia state are briefly touched upon. A "collective sample", composed of 61 cases culled from the literature, is analysed and compared with the "Fulbourn sample" consisting of 22 cases reported for the first time. Two sub-types of pseudodementia emerge, one associated with depressive illness and the other with delirium. A follow-up of the Fulbourn sample (1–4 years after discharge) showed 14 patients to be alive and 8 to show no signs of dementia. No variable except the diagnosis "non-specific psychosis" correlated with death during the follow-up period.

"Pseudodementia" is a term that refuses to go away. At the last count there had been over 30 specific publications on the topic, and the flow is not abating. It is difficult to believe therefore that the clinical phenomenon of pseudodementia exists only, as has been suggested, in the eye of the psychiatrically untrained beholder.

However, no positive definition has so far been established for pseudodementia and hence anecdotal reporting, skewed series and speculation abound. This lack of a definition is due, in all probability, to limitations in the clinical resolution of the vocabulary currently available to describe states of impaired cognition: as a consequence, any specific symptom-pattern that might characterise pseudodementia is missed out altogether.

Persistent efforts during the nineteenth century to make irreversibility into one of the hallmarks of dementia created the need for a parallel term to describe the reversible forms of cognitive impairment (Berrios, 1985). "Vesanic dementia" discharged this duty until the 1880s when Wernicke replaced it with the new term "pseudodementia" (Berrios, 1986).

During this early period, however, the concept of pseudodementia was of limited clinical use because it sailed too close to the "functional" hypothesis. In its Wernickian version it implied the presence of hysterical mechanisms, and for a time it looked as if the term was to disappear altogether. A relatively recent broadening of its clinical domain has given the term "pseudodementia" a new lease of life.

"Pseudodementia" therefore represents a collection of clinical states rather than a process, a convergence point for pathological conditions of different aetiology whose common denominator is an ability to impair cognition or to disable the mechanisms by which cognition is expressed.

The first part of this paper analyses further the concepts involved in the term "pseudodementia". We then consider a sample of 61 patients culled from the literature; then report on a group of 22 new cases and their follow-up, carried out 1–4 years after the index episodes. The two samples are compared.

The concept of pseudodementia

The term "pseudodementia" was used by Wernicke (Bleuler, 1934) to refer to "chronic hysterical states mimicking mental weakness" and this theoretical stricture made it tantamount to the so-called "Ganserian states" (Kammerer, 1975). Categories such as "vesanic dementia", "melancholic dementia" (Berrios, 1985), "melancholia attonita" (Kahlbaum, 1874) and "stupid depression" (Delasiauve, 1851; Berrios, 1981) had also been used for forms of cognitive impairment complicating a primary psychiatric disorder.

"Pseudodementia" has since gained at least three new meanings, here labelled PSD1, 2 and 3. Madden *et al* (1952) used it to refer to states of reversible cognitive impairment in subjects suffering from "involutional psychoses" (PSD1). Kiloh (1961) revived Wernicke's usage and emphasised the parody-like nature of such impairment (PSD2). A third usage is provided by the current bad habit of diagnosing delirium and other acute disorders of consciousness as pseudodementia (PSD 3). These three usages are found intermingled in the literature.

Two views are popular concerning the nature of this clinical state. Some consider pseudodementia as a genuine form of cognitive impairment (McAllister, 1981, 1983; Kramer, 1982; Janowsky, 1982; Post, 1975); others consider it a clinical mirage made possible by the vagaries surrounding the traditional semiology of dementia and by the limitations

TABLE I

Summary data of two groups of patients with pseudodementia, one group ($n=61$) culled from previous publications and the other ($n=22$) reported here for the first time

	Collective sample ($n=61$)	*Fulbourn sample ($n=22$)*	*Comparison of samples (χ^2 test, except for age)*
Age			
Mean ± s.e.m.	57 ± 14.3	73.3 ± 10.3	$t=2.74$ ($P<0.01$)
Median	59.11	72.2	
Mode	63.09	77.4	
Sex	29 M : 32 F	6 M : 16 F	1.95
Personal history			
Psychiatric illness	37 (60.0%)	12 (54.5%)	0.0608
Affective disorders	21 (34.4%)	7 (31.8%)	0.0016
Serious medical disease	9 (14.8%)	6 (27.3%)	0.97
Diagnosis of "dementia" at admission	31 (50.8%)	14 (63.6%)	0.61
Neurological findings	19[1]	6 (27.3%)	0.0047
Psychopathology			
Depressed mood	33 (54.1%)	20 (90.9%)	7.96 ($P<0.01$)
Hallucinations	11 (18.0%)	6 (27.3%)	0.37
Delusions	19 (31.1%)	12 (54.5%)	2.85
Confusion	22 (36.1%)	5 (22.7%)	0.77
Diagnosis			
Bipolar affective disorder	9 (14.8%)	5 (22.7%)	0.27
Unipolar depression	39 (63.9%)	10 (45.5%)	1.58
Non-affective illness	13 (21.3%)	7 (31.8%)	0.485
Duration of index episode			
Under 4 weeks	14 (23.0%)	0	10.221 ($P<0.01$)
1 month–6 months	33 (54.1%)	8 (36.4%)	
6 months–1 year	9 (14.8%)	4 (18.2%)	
Over 1 year	5 (8.2%)	10 (45.5%)	
Treatment with ECT	26 (42.6%)	6 (27.3%)	1.02
Outcome			
Positive	29 (47.5%)	11 (50.0%)[2]	0.025
Positive + sequelae	8 (13.1%)	7 (31.8%)[2]	2.66
Positive then relapse	11 (18.0%)	3 (13.6%)[2]	0.09
Negative	1 (1.6%)	1 (4.5%)[2]	

[1] Data available only for 39 cases

[2] Assessed within two months of discharge

inherent in the clinical instruments and biological markers designed to discriminate between real and sham impairment of cognition (Kiloh, 1961; Wells, 1979, 1982; Mahendra, 1983, 1984; Reifler, 1982; Shraberg, 1978, 1980*a*, 1980*b*; Carney, 1983; La Rue, 1982; Azorin & Mattei, 1983; Cummings & Benson, 1983; McAllister *et al*, 1982). Both views are partially correct.

Reported cases

Pertinent clinical material can be found in unlikely places: apart from studies dealing with pseudodementia as such, cases are also included in publications concerned with over-diagnosis of dementia (Marsden & Harrison, 1972; Nott & Fleminger, 1975; Freemon, 1976; Ron *et al*, 1979; Smith &

Kiloh, 1981; Garcia *et al,* 1981) or the cognitive impairment said to accompany some forms of depression (Donneley *et al,* 1982; McAllister, 1981; Cohen *et al,* 1982; Cronholm & Ottosson, 1961; Sternberg & Jarvik, 1976; Stromgren, 1977) or mania (Bond, 1980; Henry *et al,* 1973; Chiles & Cohen, 1979). Germane cases are also mentioned in association with Ganser states (Kiloh, 1961; Adler, 1981), hysterical conversions (McEvoy & Wells, 1979; Anderson *et al,* 1959), mental retardation, personality disorders (Wells, 1979), psychosocial incompetence in the elderly (Gurland & Toner, 1983) and schizophrenia (Fisman, 1982).

All told, about 209 cases seem to have been reported so far. Of these, 78 cases belong to the neurological literature and contain scanty psychiatric data, and 70 others are reported in papers which describe the statistics of samples rather than individual data. The residuum, described below as the Collective sample, includes 61 cases. We also consider a group of 22 previously unreported cases (to be called the Fulbourn sample). Depressive pseudodementias are over-represented in both samples.

The collective sample

The obvious risks of dealing with samples taken from different sources cannot be avoided in areas bereft of adequate clinical material, especially when it is important to determine usage. The first column of Table I contains data on an accumulated sample of 61 patients drawn from 22 publications. The mean age of the 29 males was 57 (s.d. 14.8) and of the 32 females 56 (s.d. 14.1).

Eight cases had a family history and 37 a personal history of psychiatric illness; 9 had a history of serious medical disease (e.g. diabetes or hypertension). Of those with a past psychiatric history, 21 had had affective disorder (15 unipolar and 6 bipolar), 5 a personality disorder, 3 schizophrenia, 2 alcoholism, 2 conversion disorder, 1 a phobic state and 1 an obsessional disorder: two further cases had previously had similar episodes of reversible cognitive impairment. Of the 39 cases for which neurological information was provided, 19 had positive signs.

At the time of the index episode, 33 patients (54%) exhibited clear depressive mood and 5 manic elation; a further 7 were "emotionally labile" but might have been suffering from mixed affective disorder. As Table I shows, a variety of psychotic symptoms were reported, including delusions in 19 cases, hallucinations in 11, confusion in 22 and one 'trance-like state'; and 43 cases (70%) showed memory impairment.

The final psychiatric diagnoses were: 39 cases of depressive illness (combined in seven cases with conditions such as hysteria, paranoia, obsessional disorder, Parkinson's disease, Ganser Syndrome and early dementia), nine cases of manic illness (one combined with a catatonic syndrome), three of schizophrenia, two of Ganser Syndrome, two reactive psychoses, and one of each of the following: paranoia, paraphrenia, neurasthenia, reactive psychosis, tardive dyskinesia and malingering.

The duration of the index episode was between 1 and 6 months for more than half the patients (see Table I).

All 26 patients who received electroconvulsive therapy improved: 29 were treated by other means and four of these did not improve (one with a Ganser State, one with hysterical conversion and two who died in hospital). Information on treatment was not published for six patients. Twenty-nine patients recovered *ad integrum*; 8 recovered with sequelae (cognitive, affective or social); 11 recovered for a short period but then relapsed into a similar state; and one did not recover. Outcome was not reported for 12 patients.

The Fulbourn sample

This sample comprised 22 cases collected retrospectively from the Psychogeriatric Assessment Unit in Fulbourn Hospital, Cambridge. The sample as a whole is compared with the Collective sample in Table I, while the individual cases are summarised in Table II.

The 6 males and 16 females had mean ages of 72 (s.d. 5.3) and 73 (s.d. 11.8) respectively. Four patients had a family history and 12 a personal history of psychiatric illness: the latter group included seven cases of affective disorder (five bipolar and two unipolar), two of hysteria, two of alcoholism (see Table III), and one case of a "similar episode". On admission, 14 received the diagnosis of "dementia" and 8 that of "pseudodementia". Six had neurological symptoms.

Examination on admission showed 20 (91%) to have depressive mood, while 12 had delusions, 6 hallucinations and 5 disorders of consciousness. Final psychiatric diagnoses were: unipolar depression (10), bipolar disorder (5), non-specified psychoses (5) and personality disorder (2).

None of the patients had an illness shorter than one month and in ten cases the illness lasted over a year (see Table I). All six of the patients who received electroconvulsive therapy responded: of the 16 (72.7%) who received other forms of treatment only one failed to respond, and died in hospital. Neuroleptics, antidepressant medication and adjuvants, and often combinations thereof, were tried on these patients. The most commonly prescribed drugs were thioridazine (5 patients), dothiepin (5 cases) and chlormethiazole (6 patients). Amongst the adjuvants the commonest were L-tryptophan and thyroxine. Information on dosage levels is very difficult to summarise, as doses were changed periodically in response to clinical needs; but the overall impression is that they were conventional in view of the age of the group in question.

Outcome analysis varies according to where the cut-off point is placed. When assessed within two months of discharge, eleven patients (50%) had a positive outcome without sequelae, seven a positive outcome with sequelae, three a positive outcome with relapse and one a negative outcome. Later evaluation of the same patients (after periods ranging from 15 to 47 months after discharge) gave a different picture. Fourteen of the sample were still alive: eight of these were "non-demented", although four

TABLE II

Summaries of the 22 cases of "pseudodementia" collected retrospectively from Fulbourn Hospital, Cambridge

Age	*Sex*	*Personal history*	*Neurological symptoms*	*Diagnosis of "dementia"*	*Depressed mood*	*Delusions*	*Hallucinations*	*Confusion*	*Treated with ECT*	*Diagnosis*	*Duration of index episode*	*Outcome (within 2 months of discharge)*	*Follow-up (15–47 months)*
81	F	Alcoholism				+	+	+		Non-specific pyschosis	Over 6 months	Negative	Dead
77	M		+	+	+					Unipolar depression	<6 months	Positive+ sequelae	Dead
89	F				+	+	+			Non-specific psychosis	<6 months	Positive	Dead
66	F	Alcoholism		+	+				+	Unipolar depression	Over 6 months	Positive+ sequelae	Demented
75	F	Unipolar depression	+		+	+	+	+	+	Unipolar depression	Over 6 months	Positive	Dead
77	M	Hystrionic personality			+			+	+	Unipolar depression	Over 6 months	Positive+ sequelae	Not demented
71	M	Physical disorder	+	+	+	+				Non-specific psychosis	Over 6 months	Positive	Dead
76	M	Bipolar disorder		+	+					Bipolar affective disorder	Over 6 months	Positive	Not demented
64	F	Bipolar disorder		+	+					Bipolar affective disorder	Over 6 months	Positive+ sequelae	Not demented
81	F			+	+	+				Non-specific psychosis	Over 6 months	Positive	Dead

85	F	Unipolar depression		+	+	+	+			Unipolar depression	Over 6 months	Positive+ sequelae	Demented
89	F			+		+		+		Non-specific psychosis	Over 6 months	Positive	Demented
66	F	Bipolar disorder		+	+	+	+			Bipolar affective disorder	<6 months	Positive	Demented
76	F	Physical disorder		+	+	+				Unipolar depression	<6 months	Positive	Not demented
68	F	Physical disorder			+	+			+	Unipolar depression	Over 6 months	Positive	Not demented
63	M	"Similar" disorder	+		+			+		Unipolar depression	Over 6 months	Positive then relapse	Not demented
51	F	Bipolar disorder		+	+					Bipolar affective disorder	<6 months	Positive	Demented
79	F	Physical disorder			+	+			+	Unipolar depression	<6 months	Positive then relapse	Demented
58	F	Bipolar disorder		+	+	+			+	Bipolar affective disorder	<6 months	Positive	Not demented
88	F	Physical disorder	+	+	+					Unipolar depresssion	<6 months	Positive then relapse	Not demented
73	M	Physical disorder	+	+	+		+			Personality disorder	Over 6 months	Positive+ sequelae	Dead
60	F	Hystrionic personality			+					Personality disorder	Over 6 months	Positive+ sequelae	Abroad

TABLE III

The Fulbourn sample ($n=22$)[1]: comparison of those who survived to follow-up (15–47 months after discharge) and those who did not

	Alive ($n=14$)[1]	*Deceased* ($n=7$)[1]	*Comparison of groups*
Sex	3 M : 11 F	3 M : 4 F	$\chi^2=0.26$
Age (mean ± s.e.m.)	71.9±11.3	78.14±6.09	$t=1.31$
Psychopathology			
Delusions	7	5	$\chi^2=2.18$
Hallucinations	2	4	$\chi^2=2.36$
Confusion	3	2	$\chi^2=0.032$
Depressed mood	13	6	$\chi^2=0.06$
Neurological symptoms	2	4	$\chi^2=2.36$
Final diagnosis			
Non-specific psychosis	1	4	$\chi^2=3.97$*
Unipolar depression	8	2	$\chi^2=0.59$
Bipolar affective disorder	5	0	$\chi^2=1.6$
Treatment with ECT			
Yes	5	1	$\chi^2=0.2625$
No	9	6	

[1] One female patient was in Australia, fate unknown

*$P<0.05$

exhibited a degree of psychosocial incompetence and were institutionalised. No difference was found between the deceased and the survivors in terms of the original variables (Table III) except that 80% of the patients with a diagnosis of "non-specific psychosis" were deceased ($P<0.05$). Likewise no difference was found between the patients with "not demented" or "demented" outcome in terms of the clinical features found in their original assessments.

Survival analysis of the Fulbourn sample by means of the product limit method (Kaplan & Meier, 1958; Lee, 1980) yielded a median survival time (MST) of 51 months. This is no different from the expected MST of healthy elderly and is significantly in excess of the expected MST of patients with dementia.

The samples compared

No overall significant difference was found between the Collective and Fulbourn samples (Kolmogorov–Smirnov two-sample test: $K=0.763$). As expected, a significant difference between the two samples was found in terms of age ($t=2.74$, d.f. $=82$, $P<0.01$). Patients in the Fulbourn sample also had significantly more neurological symptomatology ($P<0.05$) and more overt depressive mood on examination ($P<0.01$), and took longer to recover ($P<0.01$).

The similarity in the relative prevalence of symptoms in the two samples, including alteration of consciousness, delusions and hallucinations, is remarkable (Table I). It is also remarkable that a similar percentage of cases were given the diagnosis "dementia" on admission and that bipolar disorders made a significant contribution to the aetiology (see Table I).

The comparison between the two samples, however, should not be pressed too hard. The Collective sample is composed of a heterogeneous mixture of cases with a wide range of ages and diagnoses and in most cases no reported follow-up assessment. The Fulbourn sample is more homogenous in age and pathology, it was collected in a single clinical institution, and there was careful follow-up (the follow-up interval for different patients ranged from 15 to 47 months after discharge).

Since no significant differences were found between the symptom patterns of the Collective and Fulbourn samples, the two were fused into a matrix and phi coefficients estimated. Depressed mood correlated positively with presence of delusions ($P<0.01$), unipolar disorder ($P<0.001$), positive outcome ($P<0.05$) and past history of affective disorder ($P<0.05$) and negatively with confusion ($P<0.02$) and non-affective illness ($P<0.001$). Hallucinations correlated positively with delusions ($P<0.001$), confusion ($P<0.01$) and non-affective illness ($P<0.01$), and negatively with unipolar depression ($P<0.05$). Confusion correlated with unipolar disorders ($P<0.01$), non-affective illness ($P<0.01$) and positive outcome ($P<0.05$). Bipolar illness correlated positively with past history of affective disorder ($P<0.001$) and negatively with non-affective illness ($P<0.05$).

Discussion

The clinical material in this paper originates from two different sources. Cases in the Collective sample have been gathered from all the publications known to the authors and this motley provenance precludes a finer analysis of the data. However, cases were included only if there was adequate clinical information on all the relevant variables.

The Fulbourn sample was collected retrospectively but more stringent criteria were used:

1. Presence of cognitive impairment with no relevant organic disorder
2. Cognitive impairment of the type seen in dementia
3. Reversibility

In addition, all cases diagnosed as "pseudodementia" by the receiving consultant were automatically included. This ensured an even sample, but also one with a mean age significantly higher than that of the Collective sample.

Our first observation, applicable to both samples, is that there is no consensus on the use and application of the diagnosis of "pseudodementia".

Our second observation is that cases were found which illustrate at least two of the three meanings specified above. The data show a correlation between hallucinations, delusions, confusion and non-affective illness, suggesting that some of the cases diagnosed as pseudodementia might in fact have been suffering from delirium. This would correspond to the third meaning (PSD3) listed above (see case reported by Allen, 1982). It cannot be discounted, of course, that on occasions severe affective disorder might give rise to behavioural phenocopies of delirium (Bond, 1980; Swartz *et al*, 1982): this would explain the reported effectiveness of electroconvulsive therapy in cases suffering from this syndrome (Roberts, 1963; Kramp & Bolwig, 1981). Our clinical material is insufficient to help on this score.

A second group of symptoms, resembling PSD1, can also be identified. In these patients depressed mood is found to be positively correlated with delusions, unipolar illness, past history of affective disorder and positive outcome, and negatively correlated with non-affective diseases and confusion. This group probably represents the syndrome of depressive pseudodementia (see case reported by Rudorfer & Clayton, 1982).

No cluster of symptoms reminscent of PSD2 (hysterical type) was clearly identified in the sample.

Our third observation refers to the effect of age on final outcome. The Fulbourn sample shows that in a geriatric population the diagnosis of pseudodementia is no guarantee of sustained recovery. Even if full recovery is achieved after ECT there is a tendency for patients suffering from pseudodementia related to affective disorder to relapse and/or develop sequelae of various kinds. The follow-up data for the Fulbourn sample yields results not dissimilar to those reported by Murphy (1983) concerning the long-term outcome of elderly patients with affective disorder. Reports that cognitive sequelae are related to ECT (Pettinati & Bonner, 1984) are not corroborated by the Fulbourn sample, in which patients given ECT and patients treated in other ways had the same prognosis in the long term (see Table III).

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A. Bulbena, Lic. en Med. y Cir. (Barcelona), *formerly Research Fellow, University Department of Psychiatry, Cambridge*

*G. E. Berrios, MA (Oxon), MD, FRCPsych, *Consultant and University Lecturer in Psychiatry, Department of Psychiatry, University of Cambridge, Level 4, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ*

*Correspondence

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Comment

Should Plasma or Urinary MHPG be Measured in Psychiatric Research? A Critical Comment

JOHANNES G. FILSER, WALTER E. MÜLLER and HELMUT BECKMANN

Many experimental findings suggest that disturbances of noradrenergic neurons in the CNS are involved in the pathogenesis of depressive disorders. Moreover, evidence indicates that adaptive changes of central noradrenergic neurons contribute to the biochemical mechanism of action of most antidepressive treatments (Goodwin, 1984; Johnstone, 1982). Accordingly, assessing the activity of central noradrenergic neurons in depressive patients has become important in psychiatric research.

One of the most commonly used strategies for this task is determination of the norepinephrine metabolite 3-methoxy-4-hydroxy-phenylethylene glycol (MHPG) in urine or plasma, assuming that the major part of MHPG in both body fluids is of central origin (Maas *et al*, 1979). However, in a series of recent publications, Kopin *et al* have presented strong evidence that only about 20% of urinary MHPG originates from the CNS (Blombberry *et al*, 1980; Kopin *et al*, 1984a). These authors have seriously questioned the significance of urinary MHPG as a biochemical marker of central noradrenergic functions (Kopin *et al*, 1984a, b). They propose the determination of plasma MHPG levels as the "best single overall index of norepinephrine metabolic rate available from examination of plasma" (Kopin *et al*, 1984b).

While both these conclusions can be accepted, it should be stressed that they are easily misinterpreted by assuming that the determination of MHPG from the plasma is a much more reliable parameter than the determination from urine for assessing central noradrenergic functions. This is not the case: determinations of MHPG in urine or in plasma respectively are of similar value.

The important differences between the calculations of Maas *et al* and of Kopin *et al* are summarised in the Table. By measuring the jugular venoarterial differences in MHPG concentrations, Maas *et al*, (1979) found that the brain releases about 41 μg/h of MHPG into the plasma, while the total urinary excretion rate was about 65 μg/h. Assuming that all plasma MHPG is excreted in the urine, either free or conjugated, they calculated that about 63% of urinary MHPG originates from the CNS and only 37% from peripheral organs. Using the same assumptions, a similar distribution should be present in the plasma.

However, Kopin's group were able to demonstrate that about 70% of free plasma MHPG is further metabolised mainly to vanillyl mandelic acid (VMA) and that only 30% appears free or conjugated in the urine (Table). Thus, if only 30% of the 41 μg/h which originate from CNS appears in the urine, central MHPG contributes only as little as 12 μg/h to the total urinary excretion rate of 65 μg/h, the central contribution to the urinary excretion of MHPG is therefore only about 19%, while 81% or 53 μg/h of the urinary MHPG excretion is of peripheral origin. Moreover, if only 30% of plasma MHPG appears in the urine, the urinary excretion rate of 65 μg/h will be only 30% of the total turnover rate of free MHPG in the plasma. The total turnover rate of free MHPG in the plasma can be calculated as about 216 μg/h (=100%). This value, calculated by us on the basis of the experimental data given in the Table, is in strong agreement with the experimentally determined total turnover rate for free MHPG in the plasma of about 225 μg/h (Kopin *et al*, 1984b). This supports the validity of the experimental data of Kopin *et al*, (1984a, b). On the other hand, if the total turnover rate of free MHPG in the plasma is as high as 216 μg/h, the central contribution of about 41 μg/h will only amount to 19% of the total MHPG in the plasma. Accordingly, central MHPG has about the same contribution of approximately 20% for urinary as well as plasma MHPG in man.

In other words, urinary as well as plasma determinations of MHPG are of questionable value for assessing the activity of central noradrenergic neurons, since the contribution of peripheral

TABLE

Compartment	*Origin*	*100% of plasma MHPG appear in urine (1)*		*30% of plasma MHPG appear in urine (2)*	
Plasma	Central	41* (1)	63% (1)	41* (1)	19% (4)
	Peripheral	24 (4)	37% (1)	175 (4)	81% (4)
	Total	65 (4)	100% (1)	216 (4) 225* (3)	100% (4)
Urine	Central	41 (4)	63% (1)	12 (4)	19% (2)
	Peripheral	24 (4)	37% (1)	53 (4)	81% (2)
	Total	65* (1)	100% (1)	65* (1)	100% (2)

Turnover rates of plasma and urinary MHPG in healthy man in μg/h on the basis of the different assumptions of Maas and co-workers (left) and Kopin and co-workers (right). Only the turnover rates indicated by an asterix (*) have been experimentally determined. All other turnover rates were calculated on the basis of the two given assumptions and the experimentally determined turnover rates. (1) Data from Maas *et al* (1979), (2) data from Blomberry *et al* (1980), (3) data from Kopin *et al* (1984b), (4) this commentary.

MHPG is as high as 80%. Both determinations serve more as an overall parameter of noradrenergic function than as a specific indicator of the activity of central noradrenergic neurons (Kopin *et al*, 1984a, b). This is also the case in acute stimulation experiments, e.g. the clonidine test (Charney *et al*, 1982; Martin *et al*, 1984) since, due to its plasma halflife of 45–75 min, plasma MHPG reflects the average norepinephrine metabolism over an interval of several hours (Kopin *et al*, 1984a). Taking all these findings together, we agree with the recent statement of Kopin *et al*, (1984b) that "it appears evident that urinary excretion of MHPG is an insensitive measure of brain norepinephrine metabolism". However, the same holds true for plasma MHPG.

The question remains: can we explain the large variety of experimental findings of urinary or plasma MHPG as biochemical markers for some sub-types of depression or as predictor for therapeutic response in depression? Two explanations are possible. Firstly, that the metabolic conversion of plasma MHPG varies with environmental factors and might be less than the 70% originally determined by Blomberry *et al*, (1979) (see Kopin *et al*, 1984b). This would increase the central contribution to urinary MHPG and could at least partially account for the findings just mentioned. Secondly, the central and the peripheral noradrenergic systems could be connected by an interactive linkage, as suggested by Maas (1984). In this case, the relative contributions of the central and peripheral noradrenergic systems to urinary or plasma MHPG would be less important. However, even if we cannot directly correlate all these findings about urinary or plasma MHPG in depressive patients with the activity of central noradrenergic neurons, their empirical value remains (Kopin *et al*, 1984b). Thus, the determination of MHPG might still have its place in psychiatric research. For the reasons given above and because of the much larger analytical problems of plasma determination, compared to urinary determination, we would not encourage discarding of the urinary determination. The recent finding by Jimerson *et al* (1983) of a positive correlation between plasma cortisol and plasma MHPG in depressed patients mirrors very well a similar positive correlation between urinary cortisol and urinary MHPG (Rosenbaum *et al*, (1983).

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J. G. Filser, PhD, *Pharmacologist, Psychopharmacological Laboratory.*

*W. E. Müller, PhD, *Privatdozent, Head, Psychopharmacological Laboratory.*

H. Beckmann, MD, *Professor, Psychiatric Clinic. Present appointment: Professor, Head, Psychiatric Clinic, University of Würzburg, D-8700 Würzburg.*

Central Institute of Mental Health, D-6800 Mannheim, Federal Republic of Germany.

*Correspondence

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Brief Reports

Short Term Intensive Psychotherapy—A Case History

RICHARD GILLETT

There is a certain population of relatively "emotionally healthy" people whose lives are especially affected by a single issue or cluster of issues. Such people may sometimes usefully use psychotherapy which is focused intensively on the relevant problem.

Case History

Mrs A is a 36 year-old housewife and mother, who jointly owns a garage business with her husband. She was referred in February 1982 by her general practitioner, after having been admitted for a hysterectomy which was postponed at the last minute due to an upper respiratory tract infection. She and her doctor then had second thoughts, and wondered if her severe dysmenorrhoea and menorrhagia might be connected with her emotional state. She was seen four times between February and May 1982 and then followed-up two years later.

At her first psychiatric interview, she had two groups of complaints: (1) depression, tension, weariness of life; and (2) painful, heavy, irregular periods. Since her menarche at the age of nine, her menstrual cycle had mostly been irregular, 7–10/21–35. In the past few years, her periods had varied but sometimes lasted for 21 days, and were either heavy or painful or both. Primolut N tablets were prescribed in August 1981, but she did not find them helpful and after consultation with a gynaecologist, eventually decided on a hysterectomy.

Her depression had lasted for many years; she lacked interest, affect, self-confidence, and energy and her perception was dulled. She felt weary, and that her life did not have much meaning. There were no endogenous features. She was not anaemic. She also complained of a lack of intimacy with her husband, and that her 13 year-old son was truanting from school and emotionally distant at home.

Her father had died of carcinoma of the lung when she was 11, and her mother had remarried when she was 13; she felt that she had had a happy childhood, with her two older siblings and two younger half-siblings. She was born and lived her whole life in one village. At the village school she was head-girl, games captain, and head librarian; she left at 15 and then worked as an office clerk. She met her husband when she was 12-years old, and never went out with anyone else; they were married when she was aged 18. They had two children, but the younger boy had died in a road traffic accident at the age of three. There was no significant past medical or psychiatric history. On examination, she looked tense and unhappy. Her face was white and drawn; her speech and movements lacked vitality. She was intelligent and insightful.

During the initial history-taking and assessment, there was one over-ridingly important emotive issue, as evident from observation of her body language signs. When she spoke of her son dying at the age of three, her body stiffened, the muscle tension in her face increased, as if trying to stifle expression, lacrimation increased (though only just perceptibly), and her voice rose in pitch and wavered. She then lightly stroked her right cheek with the tip of her forefinger, as if wiping away an imaginary tear—a common sign which usually indicates a desire to cry at the same time as a wish not to show it. At this point, the therapist did not continue with the history-taking, but encouraged her to go on talking about the event.

David, who was three, and his brother John, four years older, had gone together to cross a road and David was run over; she told the story matter-of-factly, with no overt emotion. The therapist intervened to say that it seemed to him she had not grieved over David's death: this was clearly indicated to him by the degree of suppression of feeling, shown by the body language signs. Tears welled up in her eyes and with encouragement, she began to cry. The therapist asked her to speak directly to her son, as if he were present in the room; she began to say "why did you go?" . . . "I miss you" . . . "I miss you so much". She wept. Later, the therapist asked her if she had anything to say to life or to God. She demanded "why did you take him away from me?" As there was anger in her voice, she was encouraged to express this feeling fully, and shouted: "why did you take him away from me? . . . Why? . . . Why?" She was very angry. At the end of the session, the therapist discussed with her the difference between the acute pain of expressed grief and the chronic numb pain and hopelessness of unexpressed grief.

She was next seen two weeks later, having cancelled her appointment the week before; she said that she had spent four hours talking with her husband about David's death—a subject that had been avoided since it happened. They had felt the pain openly together for the first time, and that had created a feeling of togetherness more than at any time in the last seven years. She felt better about herself and relieved, but even though she had made good use of her therapy, and was more energetic, she still looked rather pallid and tense. The therapist considered that either there was more grief to come or that there was some other particular barrier.

In her third session, the answer became clear. She came half an hour late; her car had broken down on the road and she had spent an hour fixing the mechanics by herself. After light banter about her mechanical prowess, she talked about her first son, John, who she said was always difficult. He walked at nine months and slept very little; he was discontented and often crying. In every way, she explained, he was the opposite of David, who had been gentle, placid, and had slept through the night. John was rebellious at school, fighting or playing truant, and he seemed covertly angry at home. Once again, the therapeutic clue was in her mode of expression rather than the words themselves—there was an element of bitterness in her tone of voice as she spoke of John. The corners of her mouth turned downwards and tensed.

The therapist suggested that she had not forgiven John for David's death. He, after all, had been the older brother, leading David across the road. With no hesitation, Mrs A said that this was true, but because she felt bad about feeling this way, she had been left with many unexpressed feelings that she did not dare to feel. Once again, the therapist encouraged her to express herself openly, using her voice fully, and with licence to be irrational.

With clenched fists, she shouted: "you killed him, you killed him! It was your fault... it was your fault!... I hate you... I'll never forgive you. Never! Never!..." It was impossible for the therapist not to be moved by the fury, the hate, the pain, and the sadness. The therapist explained that in his opinion, it was better to clear it up and try to make a different relationship with John—it was not too late. But a rational explanation did not of course stop her from feeling herself as a bad mother; she had never admitted such feelings to herself before. It was only when the therapist related his own personal experience of negative feeling, that she began to accept herself as human, and was grateful for a small amount of comfort.

Her final therapeutic session was four weeks later—by her own choice. She said that after the last session, she had cried for many hours. She had gone for a long walk with her husband in the woods, told him everything, and cried with him. For two days, she felt weak and shaky. After two days, she began to feel a surge of relief, and noticed that her relationship with John was different. He appeared to act differently towards her—more friendly and enthusiastic—and she, for her part, had genuinely forgiven him. She talked to him about David's death, and he admitted to her that he had always felt guilty and had known that she blamed him.

She had had two menstrual periods since the beginning of her psychotherapy, both 7/28, not excessive and with no severe pain. Her face was less tense, with more colour; she was relieved and grateful. She was given a follow-up appointment, two years later, and her case was discussed with her general practitioner, who knew her well.

Her periods had worsened after the psychotherapy, and in August 1982 she had a hysterectomy; histology of the myometrium revealed benign leiomyomata. Her mental-emotional gains, however, had continued; she looked lively, and had no further depressive episodes. Her relationship with John became better and better; he stopped fighting and truanting at school so suddenly that his teachers wondered what had happened. She explained that he had done "anything for attention, because I had switched off from him". She was now taking him to basketball, playing tennis with him, and said "we're close as anything".

Discussion

This patient's menstrual cycle had been relatively normal during her period of psychotherapy, for the first time for many years, coinciding with a period of intense release of repressed feeling and alleviation of depressive symptoms. This concurrence is interesting (Greenberg, 1983), as is the interplay between clear organic and psychological factors.

Her case provides an example of unresolved feelings about a single life event, in someone of otherwise "stable" personality, having a profound and prolonged effect on the patient, her marital relationship and her living child. The death of a child may create in the mother "the most distressing and long-lasting of all griefs" (Gorer, 1965; Parkes, 1972).

One of the drawbacks of psychotherapy is that it often takes a long time. It is interesting to consider the possible factors which allowed for a maintained psychological change after brief psychotherapy. The most important factor was probably her basic strength of character: she had been head-girl at school and was a very capable person, with intelligence, resourcefulness, and integrity. Psychotherapeutic techniques probably affect "normal" people more than they do less integrated ones (Sargent, 1966). Secondly, she had support outside the therapeutic situation: her husband was sympathetic and genuinely supportive of her change. Thirdly, she was well-motivated (Malan, 1975). Since the major problem was fairly specific, this was an ideal case for brief, in-depth psychotherapy.

The factors in the therapy which allowed for both briefness and depth are difficult to know without personal bias, but four factors seem to stand out. The first is attention to body language: accurate perception of this may provide a quicker indicator than speech of the issues which are most important emotionally. In this case, the issue of her son dying might reasonably have been assumed to be highly likely to be important, but in others, the emotive issues are far less open to deduction.

Perceiving the signs of the body may increase the reliability of interpretation and intervention (Frank, 1979). In this case, the therapist *said that* (rather than *asked if*) she had not grieved. Such a direct statement requires experience and a willingness to be mistaken, but it may create in the patient an important, often unconscious decision, which approximates to: "there's no point in trying to keep up appearances with this person". Such a decision can save months of resistance.

The second factor is the potentially productive but rather threatening technique of actively encouraging expression of feeling, rather than talking about it (Shulman & Ream, 1983). There is a significant overlap here with the behavioural techniques of guided mourning (Mawson *et al,* 1981).

Encouraging expression of feeling can greatly accelerate the therapeutic process, but it requires experience, as well as "sensitivity in the judging of therapeutic pace" (Tillett, 1984), and should only be used in appropriately selected cases.

The third factor is the importance of what Malan (1975) calls "focality"—focusing on an objective, rather than passively following wherever the patient wants to go. Discussion of early childhood memories or of transference, for example, was unnecessary. To select such a focus, it is important for the therapist to perceive the major issue(s) accurately and to be more directive in encouraging the patient to follow a potentially productive line of thought or of feeling thoroughly.

The fourth factor is the capacity and the willingness of the therapist to "journey with the patient through the pain". This involves an empathy in feeling, combined with a human-ness of response (Frank, 1979) appropriate to the patient's capacity and personality. For the experienced therapist, this need not and should not preclude a simultaneous objectivity.

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Richard Gillett, MA, MB, BCh, MRCPsych, *Director, North Street Counselling Centre, 58 North Street, Leighton Buzzard, Beds.*

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True Auditory Hallucinations as a Conversion Symptom

CHITTARANJAN ANDRADE and SHOBA SRINATH

Hallucinations presenting as conversion symptoms have long been documented. Farley, Woodruff & Guze (1968) reported conversion hallucinations in 12 of 100 unselected post-partum cases, second in frequency to blindness among the conversion symptoms recorded. Goodwin *et al* (1971) found 8 cases of hysteria in a series of 117 psychiatric in-patients with hallucinations; of these 8 cases, most had hallucinations in more than one modality. Numerous case reports describe conversion hallucinations (Levinson, 1966; McKegney, 1967; Fitzgerald & Wells, 1977; Modai *et al*, 1980). Rack (1982) cites a case of hysterical hallucinations and adds that in Asian women, especially teenagers, the commonest cause of hallucinations is not schizophrenia but hysteria.

Fitzgerald & Wells (1977) suggested that conversion hallucinations are characterised by naivete, imaginativeness and caricature and by their evoking in the examiner a sense of levity. The concept of conversion hallucinations is currently gaining acceptance in standard texts. Nemiah (1980) writes that hallucinations, though uncommon in conversion disorder, are most frequently visual and characteristically comprise complex scenes or fragments of action that are repetitive and stereotyped and that often reproduce the scenes of a real past event of emotional significance.

It is curious that although such isolated attempts have been made to characterise conversion hallucinations, there is no discussion in the literature of the significance of true versus pseudo-hallucinations in this context. We intend in this case report to add to the growing evidence documenting hallucinations as conversion reactions and to point out certain unusual features of this case.

Case Report

K, a sophisticated 10 year-old girl with histrionic premorbid personality traits, was brought by her parents with a history of hearing voices for 9 days.

Two weeks before the onset of complaints K's favourite uncle unexpectedly died. K was heartbroken. During the funeral ceremonies she spent her time fanning the flies away from the corpse, sobbing and kissing it all the while. Over the subsequent week she remained quiet and withdrawn, slept poorly and ate less than usual.

Shortly, a fresh stress appeared. The scheduled eleventh-day death ceremonies necessitated K's missing the opening week of a new academic year in her school—something that would be taken seriously by the school authorities. K voiced her apprehensions frequently in this regard. Heightening her anxiety was the reputation for punitiveness that her school enjoyed.

When she finally attended school, she was told that her section had arbitrarily been changed. K returned home that evening and wept, complaining that her section had been changed, that she had been asked to work with strangers and that in place of a popular teacher whom she had expected, she had a teacher who was very strict.

Next day she went to school in a state of distress. As soon as she entered the door of her new class she began hearing a voice which said, "Come, come, don't be in the class". Interestingly, though her mother tongue is Kannada, the voice spoke in English—the medium of instruction in her school. K felt afraid, but entered the class nevertheless. The voice seemed to emanate from near the door, but nobody was to be seen there. The voice continued incessantly right through the day, repeating its stereotyped message like a gramophone needle stuck in a groove. K's fear grew and she developed palpitations, tremors, sweating and dryness of the mouth. The voice was that of a young lady, heard in clear consciousness with K having no ability to influence or modify it in any way. She had no idea as to whom the voice could have belonged or why it should torment her so. The voice disappeared the moment she left the class.

K attended class twice more over the next week. Each time the voice identically recommenced as she entered the class, persisted with its stereotyped message as long as she remained within and disappeared the instant she left. There were no features to suggest that the hallucinations were either functional or reflex. The content and characteristics of the hallucinations remained the same.

At home, K seized every opportunity to be pampered and to evade responsibility. She played and interacted as usual in her neighbourhood and revelled in the attention and wonder that her experiences evoked amongst those of her neighbours who had heard of the situation. However, her sleep and appetite remained impaired and she felt persistent unease and restlessness which she could not explain.

Since she was unwilling to attend class because of her frightening experiences which showed no signs of abating, her parents brought her to us.

Mental status examination revealed an anxious girl with situation-specific stereotyped auditory hallucinations as already described. She did not believe that the voices were part of her imagination or that they were "psychological" in origin. She was historically as well as cross-sectionally well in touch with reality.

Next day, the headmistress, hearing that K was experiencing some problem in her section, put K back into her original section. The hallucinations disappeared immediately and K rapidly recovered her functional ability in school. Though she later visited the "problem" class often, there was no recurrence of hallucinations. Her impaired sleep to appetite and also her anxiety and disquiet however took a further two weeks to return to normal. To date, six months after the initial presentation, she remains symptom-free.

Discussion

So well in touch with reality was K, so peculiarly situation-specific the hallucinations and so clear the gain that we never considered a diagnosis of psychosis. We favoured a diagnosis of Adjustment reaction, with predominant disturbance of other emotions—ICD 309.2 (with the hallucinations being a conversion symptom) rather than hysterical neurosis for two reasons. Firstly, the hallucinations and manipulative behaviour were merely a transient part of a longer illness characterised by agitation, anorexia and insomnia, occasioned by her uncle's death. Secondly, it is extremely unlikely that K would have manifested such symptoms due to a change in her section had her emotions not already been in a state of flux. The fourth-digit category was chosen since anxiety rather than depression predominated over most of the course of her illness.

This case has several unusual features. Firstly, it is common experience that hallucinations are unusual in children: even in psychotics, let alone those with other diagnoses. Secondly, excepting the reports of Levinson (1966) and McKegney (1967), no examples have been reported of conversion hallucinations presenting solely in the auditory modality. Thirdly, the sense of naivete is missing, as are the caricature and imaginativeness which evoke levity in the examiner as proposed by Fitzgerald & Wells (1977).

There is an interesting offshoot of this case report.

It is widely believed in major psychiatric centres in India that true hallucinations do not occur as conversion symptoms and that conversion hallucinations are, phenomenologically, pseudo-hallucinations. We do not know whether the same belief is held all over the world since no account in the literature discusses this point; however, since hallucinations were once considered to be pathognomonic of psychosis and since most standard texts even today do not include hallucinations as possible conversion symptoms, it is conceivable that there may be considerable resistance to the suggestion that true hallucinations can present as conversion symptoms.

Fitzgerald & Wells (1977) and Nemiah (1980) have suggested that conversion hallucinations have certain characteristics. However, is it right to say that conversion hallucinations are pseudo-hallucinations?

Two concepts of pseudo-hallucinations have been proposed, which have been well described by Hare (1973) and Kraupl Taylor (1981). According to the traditional German concept proposed by Kandinsky and later taken up by Jaspers, a pseudo-hallucination is a special type of imagery characterised by subjectivity, and occurring in inner subjective space. According to the traditional British concept, a pseudo-hallucination is one that is perceived through the senses but is recognised by the patient as not being a veridical perception (Sedman, 1966).

Reviewing the reports cited earlier, no hallucinations have been phenomenologically typed. The patients of Levinson (1966) and Modai *et al* (1980) experienced hallucinations originating in subjective space. Furthermore, Levinson's (1966) patient was aware that her perception was not a veridical one. Interestingly, Goodwin *et al* (1971) reported that 71% of their hysterical patients had insight into their hallucinations. These examples therefore satisfy either the one or the other definition of a pseudo-hallucination. The phenomenological status of the hallucinations described in the remaining reports is however not clear.

K's hallucinations, coming from near the door of her classroom, were located in objective space; she considered her perception to be a genuine one. Although our assessment was necessarily subjective, we felt that her level of understanding and sophistication was sufficient to consider her absence of insight significant.

We therefore suggest that on the evidence of our case, whichever definition of pseudo-hallucinations one adopts, true hallucinations can and do occur as conversion symptoms.

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Chittaranjan Andrade, MB, BS, *Resident for the course in MD (Psychiatry), National Institute of Mental Health and Neurosciences, Bangalore 560029, India.*

Shoba Srinath, MD, DPM (Psychiatry), *Lecturer in Psychiatry (Child and Adolescent Psychiatry Unit), National Institute of Mental Health and Neurosciences, Bangalore 560029, India.*

*Correspondence

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Hypomania following Cognitive Therapy

DAVID KINGDON, PAT FARR, SIOBHAN MURPHY and PETER TYRER

Clinical trials of cognitive therapy (Rush *et al,* 1977; Blackburn *et al,* 1981; Teasdale *et al,* 1984) suggest that it is an effective treatment for some forms of depressive illness. It has been suggested (Crown, 1983) that if a treatment is effective, it will also be prone to unwanted effects, whereas conversely, if the treatment has no unwanted effects it is unlikely to have any positive ones either. Physical treatments of depression carry the risk of several unwanted effects and in particular, have been shown to precipitate mania (Bunney *et al,* 1972; Lancet, 1979). We report here a new addition to the list of antidepressant treatments liable to induce mania; cognitive therapy

Case History

A widowed 57 year-old lady of Italian descent was referred by her general practitioner (GP) with symptoms of depression: she had felt tired and dysphoric since the death of her mother, two years previously. In that same year, she had moved from her home town of Blackpool to live in Nottingham; she had also had serious family problems, which included her son "bringing shame on the family" by disclosing that he was homosexual. She had no biological symptoms of depression. After the death of her husband, ten years before this episode, she had been treated by her GP for sleep disturbance, but had not been referred to a psychiatrist on that or any other occasion. There was also no family history of affective disorder. She had been prescribed flupenthixol in low dosage by her GP, eight months before assessment, but had taken this on one occasion only. She was assessed for and agreed to take part in a study comparing the efficacy of cognitive therapy, drug treatment, and self-help in depressive and anxiety disorders (Tyrer *et al,* to be published) and was allocated to cognitive therapy. Her clinical state was assessed using a structured clinical interview for DSM-111 disorders (SCID) (Spitzer & Williams, 1983) and found to be that of dysthymic disorder. Progress and treatment was assessed using Depression (Montgomery & Åsberg, 1979) and Anxiety (Tyrer *et al,* 1984) Scales derived from the Comprehensive Psychopathological Rating Scale (Åsberg *et al,* 1978), and self-ratings of anxiety and depression were recorded using the Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983). Life events in the six months before beginning treatment were recorded using a standard scale (Paykel *et al,* 1971). All assessments were made by SM, who was unaware of the treatment to which a patient had been assigned. At initial assessment, this patient had few anxiety symptoms, but a MADRS score of 16; this is consistent with the moderate degree of depressive symptoms found in dysthymic disorder and compares with a mean score of 32–34 in patients referred for ECT (Gregory *et al,* 1985). The Community Nurse (PF) administered a shortened form of cognitive therapy (Beck *et al,* 1979) with five sessions of one hour each, given over six weeks. On each occasion, the patient was given weekly activity schedules, target sheets for assessing goals in treatment, and a diary of dysfunctional thoughts to keep. She responded well to treatment, came to realise that her son's sexual orientation was not a major stigma for the family, and no longer felt guilty about it. When seen as an outpatient by PT one month after starting treatment, she had lost virtually all her depressive symptoms (Fig.). Anxiety scores did not alter significantly over this period. Over the next two weeks, her mood continued to rise; she needed progressively less sleep, and became overactive with pressure of speech, disinhibition, and flight of ideas. Nine weeks after beginning treatment, she was admitted to hospital, and was diagnosed as having mania using SCID soon afterwards. She responded well to thioridazine, 200–400 mg daily and was discharged after seven days as an in-patient, but continued day hospital care for a further month. Subsequently, she returned to a mild depressive state, similar to that at initial presentation, but six months later was symptom-free. There were no significant life events immediately before or during treatment with cognitive therapy, and the only scored item on the Life Events Scale was the onset of arguments with members of the extended family—an event that was related clearly to the onset of manic symptoms.

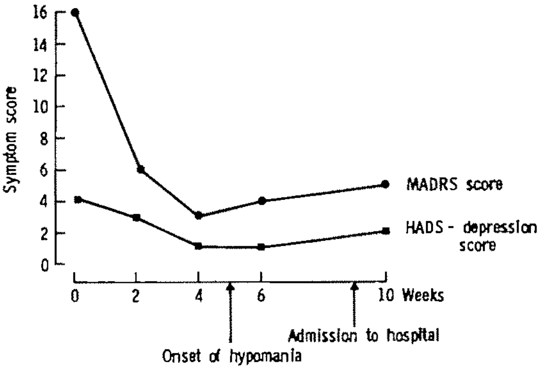

Fig. Changes in depressive symptoms during treatment with cognitive therapy

Discussion

We describe here a hypomanic episode, occurring in a woman with no previous history or family history of psychiatric illness, and taking place during the course of cognitive therapy. One of the clinical features that is sensitive to the beneficial effects of cognitive therapy is the patient's view of self, and improvement in self-esteem takes place early in treatment (Blackburn & Bishop, 1983). The onset of elevated self-esteem occurring in our patient, between four and six weeks of treatment, is consistent with an effect of cognitive therapy. However, the patient was receiving intensive contact with nurses and doctors at the same time, and this may also have contributed to the change in mood. Similar precipitation of hypomania by antidepressants, in both unipolar (Van Scheyer & Van Kammen, 1979) and bipolar depression (Bunney *et al*, 1972), can also occur after a few weeks of treatment. Although there is some evidence that life events may precipitate episodes of hypomania (Ambelas, 1979), our patient had experienced no significant new events during or immediately preceding cognitive therapy.

If, as seems to be the case, the hypomanic episode was precipitated by cognitive therapy, it supports other evidence of the efficacy of this type of treatment in depressive disorders. Although it would be wrong to regard hypomania as a hazard of this therapy, it may be wise to try and moderate the rate of improvement of self-esteem, if it appears to be taking place too rapidly during treatment.

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David Kingdon, MB, MRCPsych, *Consultant Psychiatrist, Bassetlaw District General Hospital, Kilton, Worksop*

Pat Farr, RMN, *Nurse Practitioner in Mental Health*

Siobhan Murphy, MB, MRCPsych, *Research Fellow and Honorary Registrar,*

Peter Tyrer, MD, MRCP, FRCPsych, *Consultant Psychiatrist, Mapperley Hospital, Porchester Road, Nottingham*

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Volume 142, Number 12 **December 1985**

Special Article

1395 Will Neurobiology Influence Psychoanalysis? *Arnold M. Cooper*

Regular Articles

1403 Clinical Implications of DSM-III Diagnoses of Alcohol Abuse and Alcohol Dependence. *Marc A. Schuckit, Sidney Zisook, and Joseph Mortola*

1409 Characteristics of Assaultive Patients Who Do and Do Not Provide Visible Cues of Potential Violence. *Elizabeth Decker Tanke and Jerome A. Yesavage*

1414 Liability of the Mentally Ill and Their Insurers in Negligence and Other Civil Actions. *Irwin N. Perr*

1419 Limit Setting on Drug Abuse in Methadone Maintenance Patients. *John J. McCarthy and Orin T. Borders*

1424 Mood Disorders in Left-Handed Stroke Patients. *Robert G. Robinson, John R. Lipsey, Karen Bolla-Wilson, Paula L. Bolduc, Godfrey D. Pearlson, Krishna Rao and Thomas R. Price*

1430 High Prevalence of Intermittent Acute Porphyria in a Psychiatric Patient Population. *Peter V. Tishler, Burns Woodward, Janet O'Connor, David A. Holbrook, Larry J. Seidman, Mark Hallett and Daniel J. Knighton*

1437 The Validity of DSM-III Axis IV (Severity of Psychosocial Stressors) *Mark Zimmerman, Bruce Pfohl, Dalene Stangl, and William Coryell*

1442 Self-Derogation and Adjustment in the Community: A Longitudinal Study of Psychiatric Patients. *Ronald J. Lorimor, Howard B. Kaplan and Alex D. Pokorny*

Brief Communications

1447 Sex and Race of Patients Admitted for Their First Psychiatric Hospitalization: Correlates and Prognostic Power. *Thomas E. Gift, David W. Harder, Barry A. Ritzler and Ronald F. Kokes*

1450 Age of Recognition of Pervasive Developmental Disorder. *Fred R. Volkmar, David M. Stier, and Donald J. Cohen*

1453 Hearing and Premorbid Personality in Paranoid States. *James A. G. Watt*

1456 The Relationship of Paranoid States to Schizophrenia. *James A. G. Watt*

1459 Psychoses Associated with Bupropion Treatment. *Robert N. Golden, Steven P. James, Michael A. Sherer, Matthew V. Rudorfer, David A. Sack, and William Z. Potter*

1462 French Medical Students' Opinion of Psychiatry. *Bertrand Samuel-Lajeunesse and Philip Ichou*

1467 Detoxification Recidivism Among Urban American Indian Alcoholics. *Daniel R. Kivlahan, R. Dale Walker, Dennis M. Donovan and Harold D. Mischke*

1471 DSM III Implications of the Diagnoses of Catatonia and Bipolar Disorder. *Richard K. Ries*

1475 "Hidden" Eating Disorders in Scottish Psychiatric Inpatients. *Stan P. Kutcher, Andrew M. Whitehouse and Chris P. L. Freeman*

1478 A Brief Test for Measuring Malingering in Schizophrenic Individuals. *Rex Julian Beaber, Albert Marston, Joe Michelli, and Mark J. Mills*

Clinical and Research Reports

1482 A High-Dose, Double-Blind Study of Ceruletide in the Treatment of Schizophrenia. *Jeffrey A. Mattes, William Hom and Joseph M. Rochford*

1484 Stability and Distinctness of Borderline Personality Disorder. *Alan Barasch, Allen Frances, Stephen Hurt, John Clarkin and Sandra Cohen*

British Journal of Psychiatry (1986), **148**, 106–108

Correspondence

Erotomania in an Arab

DEAR SIR,

We were interested to read the reports concerning 'De Clérambault's syndrome' or 'pure erotomania' (*Journal*, January 1985, **146**, 90–95 and *Journal*, June 1985, **146**, 661–663). We here report the first Arabian case.

A 25-year-old Arabian female, single, jobless, with borderline intelligence, had received psychiatric treatment for paranoid schizophrenia during the past nine years. Her illness started when she was 16 years old with delusions of persecution and hallucinations. She had frequent relapses, several admissions, and was treated with major tranquillisers and electroconvulsive therapy. Recovery was never satisfactory. She left school at the intermediate level, never worked, and never got married. She is a shy, over-sensitive, religious, introverted person, who had never had sexual experience or a love affair. She is the only child of conservative, religious parents. Her father died when she was one year old and she was brought up by her grandmother. Her mother remarried and has four children. Now the patient lives with her mother and stepfather and his family.

More than three years ago while attending an engagement party of a distant relative, she suddenly developed a strong belief that this relative loved her and wanted to marry her. He was a university graduate, whom she had never seen before. Since then she has been preoccupied by this false belief, and insists that he sends her messages. She heard his voice everywhere, and at the same time she had other auditory hallucinations and passivity feelings. She had sexual fantasies involving her lover. She is still convinced that he loves her despite his denial and her family showing her a videotape of his marriage, and repeated confrontations. Her condition remained unchanged with deterioration in her personality.

We agree with many others that most cases of erotomania are secondary and that the associated diagnosis here was paranoid schizophrenia.

MAGDA H. EL-BADRAMANY
MOHAMMED A. AREF
Psychological Medicine Hospital,
PO Box: 4081, Safat,
Kuwait

Neuroleptics in Culture-Bound Syndromes

DEAR SIR,

Farmer and Falkowski's illuminating description (*Journal*, April 1985, **146**, 446–448) of two West African women in whom psychotic excitement seemed to be partly triggered and maintained by their belief in bewitchment raises important questions about psychotic processes. In the cases described, fluctuating disturbances of thought, mood and behaviour persisted for several months, and were resistant to large doses of major tranquillisers and ECT. Final resolution of psychosis only occurred when the patients were permitted to take appropriate action to lift the spells. Their belief in being bewitched antedated any overt psychiatric disturbance, and in any case was shared by normal people from their own culture.

In similar vein, I recall the recent case of a young Nigerian who, after a period of unhappiness and homesickness at his new English school, developed an acute excited psychosis with protean grandiose and religious delusions, expansive, volatile mood, and persistent overactivity and destructiveness. His disturbance was unchecked by oral and parenteral haloperidol, at one stage given in doses of up to 240 mg per day. Large doses of neuroleptics maintained over several weeks produced mild drowsiness and obtundation of thought, without significant alleviation of psychotic excitement. His eventual and sudden recovery seemed to coincide with our decision to acknowledge his and his parents' belief that he was under a spell cast by another relative, and to arrange for his repatriation so that appropriate exorcism could be carried out by a local healer.

Acute florid psychoses arising in immigrants in the context of cultural alienation and threatening life events are often regarded as variants of hysteria. In such cases psychosis may represent a defence against conflict or threat, its manifestations being elaborated more or less unconsciously to correspond with the patient's idea of insanity or bewitchment. Although hysterical psychoses are usually defined as brief reactive episodes, a relatively protracted course may be common in disorders which otherwise meet criteria for hysterical psychoses, and therefore presumably have a good eventual outcome (Gift *et al*, 1985). Why should hysterical psychoses apparently be totally resistant to physical treatments when other acute reactive psychotic states typically get better quickly if arousal levels are reduced by tranquillising drugs (Lerner *et al*, 1979)? The answer I believe is that hysterical psychoses are pseudopsychoses in the sense that they are generated by ideas and experiences normal in the patient's culture, and they are probably not associated with ego-boundary disturbances. The latter may occur in true psychoses because of abnormal awareness of internally arising stimuli which many authors conceptualise as the result of a defective perceptual filter mechanism (e.g. see Johnson, *Journal*, April 1985, **146**, 429–435). In these cases, major tranquillisers probably help firstly by reducing over-arousal when this contributes significantly to defective information processing, and secondly, and more fundamentally, by directly reducing awareness of internally arising psychotogenic stimuli. Although biological mechanisms which may underlie hysterical conversion and dissociation remain a mystery, the resistance of hysterical 'pseudopsychoses' to neuroleptics suggests that they are quite distinct from those mediating true psychotic states. The apparent presence of ego-boundary disturbances as reflected by Schneiderian first rank symptoms may not reliably exclude hysteria, because elements of these may be incorporated into ideas which determine symptoms in hysterical patients who have had previous contact with psychiatry and psychiatric patients.

From the point of view of management, once a hysterical psychosis is suspected, it may be fruitless to persist with aggressive drug treatment to quell excitement. Instead, an effort should be made to understand the reminiscences from which the patient is suffering, and from which he is trying to escape through the vehicle of culturally determined ideas and disturbed behaviour. This may set the scene for effective catharsis through argument, explanation, or ritual, as appropriate to the patient's culture.

PHILIP E. HARRISON-READ

St Charles' Hospital,
Exmoor Street,
London W10 6DZ

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Cavernosal Alpha Blockade: A Treatment for Erectile Impotence

DEAR SIR,

We read with interest Professor Brindley's article (*Journal*, December 1983, **143**, 332–337) describing his treatment of erectile impotence. We employed this method at the Repatriation General Hospital, Greenslopes, and found it satisfactory.

We have since adopted modifications to the original treatment which have resulted in improved convenience to the patient. The intracavernosal injection of 30 mg of Papaverine and 1 mg of Phentolamine produces a penile tumescence which results in erection when followed by sexual stimulation within 8 hours of injection.

We have found that apparently intractable cases of impotence spanning two to thirteen years respond well. Patients have been instructed in self-injection after being observed fully at outpatients, and are thus able to become autonomous in their control of the treatment. Some have found that erections occur spontaneously without injections after three or four treatments.

Of 13 men treated this year all except two had excellent results and four did not need injections after a course of 6 cavernosal injections. They were able to maintain spontaneous erections.

Three were diabetic and one of these had no response. One man developed priapism which was successfully treated with a Tru-Cut biopsy needle.

Phenoxybenzamine was not used after 1984 because it was felt the response was not physiological. It caused erection without stimulation and did not subside after intercourse. The papaverine/ phentolamine injection allows intercourse after stimulation and subsides spontaneously after it.

LILLIAN CAMERON
PETER WOODRUFF

Repatriation General Hospital,
Newdegate Street, Greenslopes,
Queensland 4120, Australia

Epilepsy, Psychosis, Kraepelin and Bleuler

DEAR SIR,

I was very interested to read the letter by Stevens (*Journal*, September 1985, **146**, 321–322) about 'Epilepsy and Psychosis'. However, I would like to correct the attribution of "formal thought disorder, disturbances of affect and autism" to Kraepelin. He was in fact the one who coined the term "dementia praecox" with all its implications for symptomatology, age of onset and prognosis. This was replaced in 1911 by E. Bleuler's term "schizophrenias" (plural!) with formal thought disorder, disturbances of affect and ambivalence as characteristic symptoms for this group of psychoses.

CORNELIA THIELS

Free University,
Platanenallee 23,
D-1000 Berlin 19
FRG

Reference

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Anorexia Nervosa: Drop-outs from Treatment

DEAR SIR,

In the *Journal*, September, 1985, **147**, 265–271, Szmukler *et al* state, "At this stage, it cannot be assumed that dropping out of treatment is necessarily associated with a poor eventual outcome. It is possible that significant benefit may be derived from only a few treatment sessions or that some patients who are making good progress feel that no further help is required." Is there not a third possibility, namely that, irrespective of eventual outcome, at the time of dropping out patients feel, rightly or wrongly, that they are deriving no material benefit from treatment?

MAURICE SILVERMAN

Clarence Rooms,
Our Lady of Compassion Hospital,
Preston New Road,
Blackburn BB2 7BG

CORRECTION

The ***Correspondence*** running heading on page 581 (*Journal*, November 1985) should read *British Journal of Psychiatry*, (1985), **147**, 581–587.

A HUNDRED YEARS AGO

Gloucester and the Beginnings of the RMPA

The French psychiatrist, Parchappe, who visited England in 1847, reported on another remarkable innovation at the Gloucester Lunatic Asylum, namely the creation of a small self-governing unit:

"This is quite an exceptional arrangement. The patients who work in the gardens occupy special quarters consisting of a kitchen-refectory with an open fire and a dormitory with 14 beds. The patients live here by themselves; the door is open directly to the gardens and is outside the asylum wall. They are supervised only by the head gardener who lives in a cottage at some distance. They go to bed at 8, get up when they like. They come and go freely just as they wish. If they wish to go into the town they have only to ask the gardener's permission. The establishment provides them with meat, bread and beer, and the gardener gives them fruit and vegetables; they do their own cooking and run their household for themselves.

The medical superintendent claims that no inconvenience of any kind has resulted from this peculiar arrangement, and this seems to show how very far one can go in introducing into institutions conditions as nearly as possible resembling those of ordinary life."

Reference

Journal of Mental Science (July 1961) Vol. **107**, No. 449, p. 613.

British Journal of Psychiatry (1986), **148**, 109–111

Book Reviews

The I. By NORMAN N. HOLLAND. New York: Yale University Press. 1985. Pp. 390. £30.

Holland is a literary critic with a sophisticated understanding of psychoanalysis and other areas of psychology. This book is wide-ranging exploration of his theme of the continuity in a person's development of the experiencing active self. He presents his 'identity theory', drawing on Lichtenstein's idea of identity as 'theme and variations', combined with his own idea of identity as consisting an *agency,* trying out strategies, hypotheses, behaviours, which results in *consequences,* through feedback, all of which is *represented* by self and others. He illustrates his thesis with studies of the thematic continuity in the lives of writers—Scott Fitzgerald and G. B. Shaw—and in Freud's case study of the Ratman. He also examines the continuity between the Little Hans of Freud's study and the life of the later Hans who became an eminent opera director in New York. A particularly interesting illustration is that of the case discussed by Robert Lifton of a man subjected to Chinese 'thought reform', who ostensibly changed his attitudes radically; Holland shows the thematic continuity between the personalities before and after the brainwashing.

This leads to his model of the mind as a chain of hierarchical activities of feedback systems, with a 'theme and variations' identity governing at the top. Like Lichtenstein, he sees identity maintenance as a fundamental principle, but for Holland this does not mean that identity exists *in* a person. Rather, he is demonstrating through his examples that it is *possible* to formulate an identity theme for a given person. The notion of identity is a way of enquiring into human actions. Identity is created *between* Holland and his subject. This activity of identity creation is seen as representative of the way a person is continually engaged in a dynamic relationship with his or her culture, actively creating meaning.

Taking Winnicott's 'squiggle game' as a model for the creation of shared meaning, he argues that "a psycho-analytic explanation draws on both the creation of a shared verbal space through free association and a thematic analysis of that space". He points out that in recent years this has become a more prominent model within psycho-analysis, replacing earlier assumptions that analysis was a seeking after an objective truth. Referring to "the betweenness of a self I once thought autonomous" he suggests that this reasoning "throws everything into betweenness—leaving us no mooring outside or beyond the sea of human relations." (p. 288).

A good psychological theory is reflexive, explaining the activities of its author. Holland is explicit that his own "needs for certainty and consistency are fierce indeed" and this is apparent in the way his book covers so many areas in his serch for synthesis. He moves easily through literature, psycho-analysis, academic psychology and philosophy of science—his discussions of the latter being, to my mind, some of the best sections of the book.

Drawing on the contributions of a number of philosophers of science, Holland argues for the importance of holistic pattern analysis in the human sciences. In this method, testing takes the form of finding new data to converge around a given hypothesis or theory; in the manner of Sherlock Holmes, a central idea is arrived at which bring coherence to the previously disparate data. He is critical of some academic psychologists for their adherence to a simplistic and outdated paradigm of science, in assuming a reality 'out there' which can be studied objectively—pointing out that in physics and other 'hard' sciences, it is accepted that the reality which is studied is created by a dynamic interaction *between* the observer and the external world.

The book contains much that is original and thought-provoking, and the reasoning is subtle. It is a major contribution to an exciting area of converging interests—which, as evidenced by the very successful inter-disciplinary Self and Identity Conference (1984, Cardiff), is a focus for much creative contemporary thinking. However, it is a long book, at times bordering on the verbose and some ideas are not stated as clearly as they could be. The style is thoroughly American, involving strange acronyms, like DEFTing and ARCing, and a variety of neologisms such as 'theming' to refer to the act of drawing out themes.

PHIL MOLLON, *Senior Clinical Psychologist, Tavistock Clinic, London*

Recent Advances in Clinical Psychiatry. Vol. 5. Edited by KENNETH GRANVILLE-GROSSMAN. Edinburgh: Churchill-Livingstone. 1985. Pp. 277. £22.00.

The fifth volume in this series of *Recent Advances* will no doubt justly become essential reading for trainees and senior psychiatrists, as have the previous four volumes. It is a pity that the title of the series is so contentious. It could be argued that, with one or two exceptions, the chapters fall into two categories; first there are those which describe real advances in knowledge that have as yet no clinical applications, and second those which are clinical but do not represent a recent advance. I was prompted to look at a volume in my collection with a similar title (*Recent Progress in Psychiatry*) but published in 1950, and was not really surprised to see that the same state of affairs existed then, although, with hindsight, much of what must have seemed like real advances was subsequently found to be wrong. It only goes to show how very difficult it is to identify important new ideas and results at a time when they are still recent but are secure enough to be called advances. *Current Themes* would be a better title (but *Recent Advances* is a consistently better book).

This volume contains an excellent chapter on neuropeptides by Mackay, and a chapter on new brain imaging techniques by Trimble, both of which fall into my first category. Also in this category is a chapter by Checkley on biological markers in depression which is an excellent summary of the latest neuroendocrine research. It is unfortunate that this chapter should have so completely escaped the editor's pen as to make it almost as difficult to read as a daily newspaper.

Chapters in my category 2 include those by Weller on the sequelae of head injury, and by Gelder on cognitive therapy, which, although well-written and interesting, cannot really be described as recent advances. The same applied to Gordon's chapter on psychosocial aspects of drug abuse. Two chapters on psychosomatic medicine, one by Lloyd and the other by Greer on cancer, testify to the growing interest in this once neglected field. Littlewood and Lipsedge's chapter on culture bound syndromes criticises the psychiatric colonialist's approach to transcultural psychiatry and gives, what I take to be, a more correct social anthropological perspective. For the uninitiated to anthropological jargon it is sometimes hard going but if, like me, you could never understand why people were bothering to teach you about these rare syndromes, it is well worth making the effort. Child psychiatry is represented by a chapter on drugs in children's disorders by Kaplan and Kolvin. Two chapters do seem to be about advances with clinical relevance. Leff's chapter on the family treatment of schizophrenia describes the exciting work and excellent results in this field obtained by his own group and others and gives a balanced critique. Hallstrom combined the recent advances in the understanding of the mechanism of action of benzodiazepines with the increased clinical awareness of their adverse effects, particularly dependence, which is beginning to lead to limitations on prescribing. This may be an advance or a retreat; in our present state of knowledge it is sometimes difficult to tell between them.

C. THOMPSON, *Senior Lecturer in Psychiatry, Charing Cross and Westminster Medical School, London*

The Borderline Spectrum: Differential Diagnosis and Developmental Issues. By W. W. MEISSNER. New York: Jason Aronson. 1984. Pp. 499. $35.00.

In this book Dr Meissner, a psychoanalyst from Boston, reassesses the borderline syndrome in terms of historical and theoretical background, differential diagnosis and aetiology (genetic, organic, developmental and family). He then goes on to lay down tentative guidelines for a new unitary theory of borderline psychopathology.

The book is learned and encyclopaedic. Meissner assesses the work of a large number of authors, from several different branches of psychiatry, and pays attention to childhood and family issues. The language of the book seemed to this reviewer to be unnecessarily complex, and consequently hard to follow. Furthermore it is repetitive, with ideas being restated in consecutive paragraphs, and in consecutive chapters as well. It is as though the author does not expect the reader to have digested and remembered what he has just read. Some chapters, in particular the one on assessment for psychoanalysis, present lists of criteria from several authors, with little critical analysis of these contributions.

In his theoretical review the author views suspiciously any contribution associated with the Kleinian school. He omits to discuss the work of any prominent Kleinian writers on this subject, such as Rosenfeld, Rey, Steiner or Segal. Such an omission needs to be carefully justified, not simply presented as a *fait accompli*. Also he sees object-relations theory as a theory of relations with *external* objects, which seems to be rather less than half the story.

There are some good chapters in the book, in particular the one dealing with developmental issues, which describes very clearly the important stage of "separation-individuation".

It is not easy to write about borderline personalities. Overall the author seems to have fallen into one of the traps in store for those who enter this particular debate, namely the temptation to write about the whole of psychoanalysis and psychiatry. Consequently the book, like the patients in question, lacks a coherent identity. I cannot recommend it for the individual reader. Those interested in this area would be better served by reading a clearer review of the subject (such as that by Stone—*The Borderline Syndromes*), and then going on to the relevant original texts.

MARK BERELOWITZ, *Registrar,*
The Maudsley Hospital, London

Emerging Dimensions of Sexology: Selected Papers from the Sixth World Congress. Edited by R. TAYLOR SEGRAVES and SERWIN J. HAEBERLE. New York: Praeger, 1984. Pp. 355. £45.00.

This is a collection of selected papers from the Sixth World Congress of Sexology held in Washington in 1983. Topics covered included the history of sexology, childhood sexuality, diagnostic evaluation of erectile disorders, psychotherapy of sexual dysfunction, surgical interventions, physiological substrates of sexual behaviour and transcultural studies. The quality of the contributions varies greatly, from reports of new advances to papers which seem to be no more than a conference ticket. Of particular interest to this reviewer was a paper on psychophysiological assessment of erectile dysfunction, and another on erectile responses in men with diabetes which suggests that even those without frank erectile difficulties have impaired erectile responses when studied under laboratory conditions. There is also a useful review of the factors associated with good and poor responses of trans-sexuals to sex reassignment.

Overall this is a disappointing volume, which does not do justice to the high quality research that some workers are carrying out in this field at the present time. Since the better contributions will doubtless be published elsewhere, and given the price of this book, few psychiatrists will wish to purchase it.

KEITH HAWTON, *Consultant Psychiatrist and Clinical Lecturer, Warneford Hospital and University Department of Psychiatry, Oxford*

Psychotherapy and the Religiously Committed Patient. Edited by E. MARK STERN. New York: The Haworth Press. Pp. 158. $16.95 (hard); $12.95 (soft).

This volume is comprised of 16 presentations by a variety of therapists and is the third in a series relating to the interplay of psychotherapy and religion. Considering it in the light of the more usual problem of the day—the patient who lacks any value system—it brings into focus the problems which present to those who do.

It highlights the problems presented to the therapists when they faced with patients whose value system is very different to their own and offers some sound advice on how the therapists may be able to work with the symbolism which lies beneath the religious overlay. At the same time it challenges the therapists who maintain that they have no religious values but whose psychoanalytic theory has really become their divine dogma. It points to the fact that if therapy is to have a goal, it must be to implement values and beliefs into action. But where are the values and beliefs to come from?

Religious questions are fundamentally questions of meaning of one's life and in one's life and not merely a question of right and wrong in the moralistic sense. The therapist needs to have some philosophy of life if he or she is to challenge the more bizarre forms which religious fervour appears to take in these days. At the same time the therapist is also faced with the Equus syndrome—what is to replace the patient's glorious obsession?

This book will be a help to the therapist who is keen to come to grips with this area of his or her patient's life and it also contains some interesting sidelights on the practice of therapy in general.

LOUIS MARTEAU,
The Dympna Centre, London

Individual Therapy in Britain. Edited by WINDY DRYDEN. London: Harper & Row, 1984. Pp. 343. Paper £8.95.

By discipling his authors and using his contributions to give context, the editor has produced a remarkably systematic book with none of the liquorice allsorts quality of the conventional contributed book. Individual enthusiasts cover a reasonably full range of therapies: dynamic, person centred, personal construct theory, existential, gestalt, transactional analysis, rational emotive, behavioural psychotherapy and what might be called systematic eclectic. Each author dutifully and usefully begins by giving a brief history of the development of their favoured form of therapy and proceeds to discuss its underlying assumptions, techniques and model of change. Inevitably, such accounts are massively condensed but they will serve as lively, basic introductions, informative for both students and practitioners.

In a second section the editor compels his contributors to ponder more deeply, by instructing them to write a chapter on the limitations of their chosen approach to therapy. In a third section the contributors rate their chosen therapy on a number of dimensions—objective/subjective, affective/cognitive and so on. The different approaches are then compared in terms of these ratings. The editor somewhat loses his nerve at the end of this section and the comparative discussion is truncated for fear it prove odious.

The book's weaknesses comprise mostly errors of omission rather than commission. Neither the editor in his opening chapter on the arena of psychotherapy, nor the contributors, discuss the political context and implications of psychotherapy, thus missing many of the significant issues covered in the comparable work of Pilgrim (*Psychology and Psychotherapy*, 1983). Nevertheless, the book is valuable, not just because (unlike the deluge of American texts) it speaks from and to the British psychotherapeutic field but because it speaks thoughtfully and to some purpose.

D. BANNISTER, *Psychologist, High Royds Hospital, Yorkshire*

Children Growing Up. Edited by ALAN BRANTHWAITE and DON ROGERS. Milton Keynes: Open University Press. 1985. Pp. 270. £5.95.

This is a book on child psychology written by nearly a score of different psychologists employed by the Department of Psychology of Keele University. Sloboda on perception (two chapters), Hutt and Trueman on the genetic basis of intelligence and on psychological aspects of cerebral anatomy, physiology and pathology (three chapters) and Hope MacDonald on sex differences in cognitive ability, are excellent in that they provide well-written informative summaries of their subjects. Hartley, on how people comprehend and how they remember, Hunter, on differences between cultures on aspects of memory, Gellatly, on some developments in Piagetian psychology, and Rogers, on language, are of some limited interest. The remainder of the book, more than half of it, contains chapters which are either indifferent, irrelevant or frankly bad. The worst contribution is by Hegarty who appears to accept uncritically the aetiological role of psychological stress in causing cancer and in an anecdotal manner extols the virtues of psychotherapy in overcoming crippling physical illness. A close second is that by Hill on abnormal personality development. He seems very unclear about 'personality disorders' in childhood and writes poor accounts of two uncommon psychiatric syndromes, 'early childhood autism' and the 'hyperkinetic syndrome'.

There is some uniformity in presentation, and some cross referencing between chapters, which creates a good impression, but many minor errors in the text, which has the opposite effect. The editors have been rather unwise in dividing the book into four sections, in view of their content, which appears somewhat incongruous in relation to what the sections are called, particularly in the case of the first three respectively: social, cognitive and personal domains. One contributor, Helen Graham, comes over as pushing anti-sexist views rather too enthusiastically, and another, Hartley, rather spoils his otherwise interesting article with esoteric terms such as 'metacognition' and 'comprehension monitoring'.

In a book which purports, at least on the cover at the back, to provide a 'coherent introduction' to child development, there are far too many omissions. There is a lack of historical perspective. Insufficient attention is paid to classical and operant conditioning. Piaget's view that representations in cognition, language and symbolic functioning, are firmly based on a foundation of sensori-motor intelligence is not emphasised sufficiently. The emotional development of the child is inadequately described. Little cognissance is taken of the wealth of cross-sectional and longitudinal studies of child development which now exists. The use of scales to measure intelligence and behaviour problems which has provided useful information on individual differences is largely ignored.

Psychiatrists may find one or two of the chapters of some interest but this book falls far short of a useful introduction to child development.

IAN BERG, *Consultant Child and Adolescent Psychiatrist, The General Infirmary at Leeds*

The Coping with Depression Course. By PETER M. LEWINSOHN, DAVID O. ANTONUCCIO, JULIA L. STEINMETZ and LINDA TERI. Eugene, Oregon: Castalia Publishing. 1984. Pp. 213. $14.95.

The course is based on a social learning approach to depression and is intended to teach group behaviour therapy of depression to experienced mental health professions. The four sections provide background information, criteria for the selection of instructors and participants, a detailed account of the course and ways of dealing with problems which may arise during therapy, and research findings. Appendices give examples of rating scales, of media adverts and letters to professional colleagues. A detailed "Participant workbook" is included and the authors recommend that instructors and participants become familair with Lewinsohn *et al's* *Control your Depression* (1978, Prentice Hall) which offers clients instruction on how to improve the skills necessary to combat depression. The course comprises 12 sessions of two hours over eight weeks, with two follow-ups at one month and six months after treatment. These follow a set format and progress from a theoretical introduction to the teaching of relaxation, scheduling pleasant activities, constructive thinking, social skills and ways of maintaining gains and developing a life plan.

An asset of the book is its clear and systematic presentation. However, one cannot help feeling that therapy and depressive illness are being trivialised. The authors say that the course is not therapy or counselling. Why then go through elaborate intake procedures, state that the course is "specifically designed to alleviate depression", undertake outcome studies and quote high success rates? It is suggested that patients with bipolar depression and acute suicidal tendencies (with concurrent treatment) and those with unipolar depressions would have an 80% chance of improvement. The opinion of the reviewer is that the course would be suitable only for very mild or perhaps recovered depressions.

I. M. BLACKBURN, *Top Grade Clinical Psychologist, MRC Brain Metabolism Unit, Royal Edinburgh Hospital*

Psychological Aspects of Cancer. Edited by M. WATSON and T. MORRIS. Oxford: Pergamon. 1985. Pp. 99. £18.00.

This is a collection of papers presented at a conference on 'Psychological Aspects of Cancer' in 1983 at Kings College Hospital, London. The aim of the conference was to encourage people "from professions with an interest in psychological aspects of cancer to meet for an exchange of views".

There is an interesting overview of Dr Pettingale's work at the Raine Institute which is concerned with the search for physiological correlates of mental phenomena. This contrasts with the much more common questionnaire type of enquiry in vogue in this field. The other fashionable phrase now being used widely is "Quality of Life". Paradoxically, various projects purport to 'measure' and quantify this quality, surely a *non sequitur*, after the diagnosis of cancer and/or during and following treatment. H. B. Devlin, a surgeon writing on psychological and psychiatric aspects of surgery, pleads for "Psychiatrists to be taught to come and help surgeons"!

Many of the terms used are not defined and some old-fashioned and erroneous notions are implied by them. For example, the word 'stress' is used as if it were necessarily bad and to be avoided. 'Hopelessness' and 'hopefulness' are undefined and in a paper by Stoll, 'hopefulness' is presumed to be present when a person is not going to die immediately, and 'hopelessness' when the individual believes that they are certain that they are going to die. The papers originating in the Kings College Unit generally try to demonstrate the effects of psychological attitudes on 'survival', after the diagnosis and treatment of cancer. There are no studies in which an attempt has been made to discover what, if anything, increases the ability of an individual to 'survive' as an integrated fulfilled adult.

The title is *Psychological Aspects of Cancer*, but the psychological aspects considered are limited. It is, however, worth reading because of the general questions that it raises about the validity of 'research' in this area and any project which promotes a debate amongst the many different professionals working in this field is to be encouraged. The price of the book seems excessive at £18.00.

LAWRENCE GOLDIE, *Consultant Medical Psychotherapist, The Royal Marsden Hospital, London*

Mental Health Care and Social Policy. Edited by PHIL BROWN. London: Routledge & Kegan Paul. 1985. Pp. 416. £25.00, £12.95 (paperback).

Readers expecting a book concerned with a discussion and debate on mental health social policy issues in this country will be disappointed. The contents of this volume are (with the exceptions of accounts of policy issues in China and Italy) entirely concerned with mental health policy and practice in the USA. All of them have appeared before—in journal or other form. About three-quarters of them having appeared in the late nineteen-seventies and the remainder in the early nineteen-eighties. (The most recent being 1982). Diverse issues are discussed, but the main thrust of the contributions is the by now familiar and well-worn theme of the paucity of state community psychiatric services in the USA and the stigmatising effects of monolithic state institutions. Some very well respected names appear in this collection of papers (Cocozza and Steadman on prediction on psychiatry; Scull on the rise of the asylum; Rothman on its enduring nature; and Scheff on psychoactive drugs and mental health policy). Lovell's somewhat uncritical espousal of the 'Italian Experience', seems now to be rather out of date in the light of more trenchant examinations (for example Jones and Poletti—*Journal,* April 1985). This volume is not without interest to the student of comparative health care policies but my guess is that it will be of less interest to practising clinicians and their colleagues in the UK. The value of the work as a whole is lessened by the absence of an index.

HERSCHEL PRINS, *Formerly Director, School of Social Work, University of Leicester*

On Learning from the Patient. By PATRICK CASEMENT. London: Tavistock. 1985. Pp. 244. £12.00 (hb), £6.50 (pb).

Patrick Casement is a training psychoanalyst within the independent group of the British Psychoanalytical Society. In this book he sets theory in its proper place, as a helpful framework for the therapist, but not to be used to obscure the understanding of patients' psychical reactions and needs, nor as a weapon to defend the therapist's narcissism. It is not an eclectic book but advocates a highly disciplined approach which paradoxically may free the patient from fixed patterns of feeling and action and should free the therapist from regurgitating hack interpretations. The chapter on listening without preconception and with a desire to learn from the patient contains useful illustrations by analogy. The discussion of interactive communications synthesises the present state of knowledge within the British School of Object Relations Theory. The account of countertransference is succinct, and Casement stresses the therapist's ability to be able to respect feelings and experiences that are not his own. "To resonate in dissonant harmonies." The chapter on the treatment of despair and other difficult psychic states separates the inappropriate use of support and reassurance from the timely use of interpretation and containment.

For Casement, any gain in cognitive insight must be matched for the patient by his experiences of (a) a feeling of structure and containment within the treatment; (b) a responsive therapist who is both non-intrusively available and who has the humility to hear promptings about what might be going awry in the treatment. The career student should read this important book early in his first year and re-read it in his final year.

PAUL O'FARRELL, *Consultant Psychotherapist, Royal Edinburgh Hospital*

Research in the Schizophrenic Disorders: The Stanley R. Dean Award Lectures. Vol. II. By ROBERT CANCRO and STANLEY R. DEAN. Lancaster: MTP Press. 1985. Pp 332. £47.50.

The Stanley R. Dean Award Lectures are given on an annual basis by scientists who have made major contributions to research on schizophrenia. Twelve of the lectures given between 1962 and 1982 are published in this volume. At the time that they were given the lectures did not report new findings. In general they consisted of an account of the authors major work set against the relevant background. The book therefore does not present a complete or up-to-date account of research findings in schizophrenia. Much of the material has been widely published elsewhere but it is a pleasure to read it in the form of the polished essays provided by some of the distinguished contributors. The chapters of Wing and Rosenthal in particular both present reports of their extensive studies in a clear concise manner which conveys their own enthusiasm for their subjects. Although Kety's lecture on biochemical studies in schizophrenia was the earliest published in this book it has stood the test of time remarkably well. His account of the limitations and possibilities of various methods of research in schizophrenia is the best I have read and I would warmly recommend it to those engaged in this field. Carlsson's chronological description of the development of pharmacology of schizophrenia since the 1950's vividly conveys the fascination of the subject. Rainer's careful summary of Kallmann's contribution to the genetics of schizophrenia provides access to interesting information which is not readily available.

It is customary for those giving distinguished guest lectures to present their subjects in a relatively positive manner and the contributors to this series are no exception. When the lectures are read one after another, their optimism has a rather relentless quality. I suspect that a number of readers might welcome a little caution and doubt and certainly some will make a mental note of the evident inadvisability of referring to a breakthrough that is just around the corner if there is any possibility of one's lecture being re-published in ten or twenty years time. This book is enjoyable but of slight practical value. Those with a limited budget are unlikely to find it a worthwhile purchase for a library but it would make a very suitable, although not ungenerous, gift for persons such as visiting speakers.

EVE C. JOHNSTONE, *Member of Scientific Staff and Honorary Consultant Psychiatrist, Northwick Park Hospital and Clinical Research Centre, London*

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Index to Advertisers

Pharmaceuticals

The Boots Company plc	*facing* p 46
E. R. Squibb & Sons Limited	*facing* p 46

Clinics, Hospitals and Nursing Homes

Bowden House Clinic	p iv
Charter Clinic	*inside back cover*

Surgical and Medical Appliances

Ectron Limited	p ii

Booksellers and Publishers

Oxford University Press	p iii
The Royal College of Psychiatrists – Gaskell	*facing* p 47

Appointments

Alberta Hospital Edmonton	p ii
British Columbia Ministry of Health	*facing* p 47
Edmonton General Hospital	*facing* p 87
The Home Office	p iii
University of Maryland	p iii

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THE BRITISH JOURNAL OF PSYCHIATRY

January 1986 Volume 148

Papers

The Measurement of Social Behaviour in Psychiatric Patients: An Assessment of the Reliability and Validity of the SBS Schedule; *Til Wykes and E. Sturt* 1

Life Events and Schizophrenia: A Saudi Arabian Study; *M. A. F. Al-Khani, P. E. Bebbington, J. P. Watson and F. House* 12

A Validity Study of a Psychiatric Screening Questionnaire (SRQ-20) in Primary Care in the City of São Paulo; *Jair de Jesus Mari and Paul Williams* 23

A Baseline Study on Mental Disorders in Guiné-Bissau; *Joop T. V. M. de Jong, Guus A. J. de Klein and Sineke G. H. M. M. ten Horn* 27

Outcome of Patients Committed to Hospital under the Mental Health (Scotland) Act 1960; *A. A. McKechnie, A. Corser and V. R. McMillan* 33

Adverse Drug Reactions to First- and Second-Generation Antidepressants; A Critical Evaluation of Drug Surveillance Data; *L. G. Schmidt, R. Grohmann, B. Müller-Oerlinghausen, H. Ochsenfahrt and P. S. Schönhöfer* 38

Mydriatic Response to Topical Naloxone in Opiate Abusers; *A. H. Ghodse, T. H. Bewley, M. K. Kearney and S. E. Smith* 44

Neuroleptic Malignant Syndrome; *R. J. Abbott and L. A. Loizou* 47

Imipramine and Amitriptyline Plasma Concentrations and Clinical Response in Major Depression; *James H. Kocsis, Israel Hanin, Charles Bowden and David Brunswick* 52

Raised Plasma Cortisol Concentrations are a Feature of Drug-Free Psychotics and are not Specific for Depression; *J. E. Christie, L. J. Whalley, H. Dick, D. H. R. Blackwood, I. M. Blackburn and G. Fink* 58

Dexamethasone Concentrations and the Dexamethasone Suppression Test in Psychiatric Disorders; *Howard Morris, Vaughan Carr, Judy Gilliland and Michael Hooper* 66

Depression, Urinary Free Cortisol Excretion and Lymphocyte Function; *Ziad Kronfol, J. Daniel House, Joseph Silva Jr., John Greden and Bernard J. Carroll* 70

Hormones, Mood and Sexuality in Lactating Women; *E. M. Alder, A. Cook, D. Davidson, C. West and J. Bancroft* 74

Computed Tomography in the Elderly: Changes over Time in a Normal Population; *Jonathan M. Bird, Raymond Levy and Robin J. Jacoby* 80

Pseudodementia: Facts and Figures; *A. Bulbena and G. E. Berrios* 87

Comment

Should Plasma or Urinary MHPG be Measured in Psychiatric Research? A Critical Comment; *Johannes G. Filser, Walter E. Müller and Helmut Beckmann* 95

Brief Reports

Short-Term Intensive Psychotherapy – A Case History; *Richard Gillett* 98

True Auditory Hallucinations as a Conversion Symptom; *Chittaranjan Andrade and Shoba Srinath* 100

Hypomania following Cognitive Therapy; *David Kingdon, Patt Farr, Siobhan Murphy and Peter Tyrer* 103

Correspondence 106

A Hundred Years Ago; *researched by Henry Rollin* 108

Book Reviews 109

Notice to contributors, subscribers and advertisers inside front cover

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The Northwick Park Study of First Episodes of Schizophrenia

I. Presentation of the Illness and Problems Relating to Admission

E. C. JOHNSTONE, T. J. CROW, A. L. JOHNSON and J. F. MacMILLAN

Collaborators: Drs B. Alapin, V. Baraniecka, U. Baruch, C. Benedek, M. Bowman, J. Bradley, J. Bruce, M. Carney, J. Candy, B. Chester, P. d'Orban, G. Edwards, K. Granville-Grossman, J. Hailstone, J. Hajioff, R. Henryk-Gutt, H. Hershon, Z. Huq, P. Jeffreys, M. Joyston-Bechal, W. Knapman, C. McEvedy, S. Mann, S. Montgomery, G. Nanayakkara, D. Owens, D. Pariente, R. Pinto, D. Pitcher, P. Pilkington, J. Price, R. Priest, M. Salasa, A. Shah, F. Sebastian-Pillai, H. Sergeant, G. Silverman, S. Spencer, J. Stead, C. Tonks.

Patients referred over 28 months from nine medical centres for a trial of prophylactic neuroleptic medication following first episodes of schizophrenic illness (462) were assessed with the Present State Examination, WHO scales for disability, past history, and sociodemographic factors, and a rating of disturbed behaviour; 253 fulfilled the study criteria; of the 209 who did not, 54 did not meet the diagnostic criteria, 65 had a history of a previous episode, and in 15 the psychotic illness was found to have an organic basis. The interval between onset of illness and admission varied widely, but was often more than one year and associated with severe behavioural disturbance and family difficulty e.g. in arranging appropriate care. Current arrangements for initiating management of first schizophrenic illnesses are frequently unsatisfactory.

Little systematic information has been collected on the mode of onset, presentation, and early course of schizophrenia. While data on age of onset (Noriek & Odegard, 1966), rates of first admission (eg Dean *et al*, 1981), psychopathological aspects (Gillies, 1958: Chapman, 1966), and outcome (Cooper, 1961; Nyman & Jonsson, 1983) are available, there is no formal study of the duration and nature of the disturbance preceding first admission. Nor have the circumstances of admission been systematically examined. Similarly, while it is established that neuroleptic medication is effective in preventing relapse after discharge (Leff & Wing, 1971; Hirsch *et al*, 1973; Hogarty *et al*, 1973; Rifkin *et al*, 1977), a small proportion of patients remain well without active medication. If there is a group who experience only one or infrequent episodes of illness, such patients would be under-represented in studies of the generality of schizophrenic episodes, and thus the prophylactic value of neuroleptic medication may be exaggerated.

We examined the prophylactic effect of neuroleptic medication following first schizophrenic episodes in a large sample of patients, intending to assess the early course of the illness and the determinants of satisfactory outcome with and without active medication. We also studied the nature of the behavioural disturbance and social difficulties at presentation and the early outcome in clinical, social, and judicial terms, as well as the relationship of expressed emotion (EE) in the family to relapse following a first episode. This paper describes the nature and selection of the total referred sample of 462 cases and the difficulties occurring in the interval between onset and admission.

Method

To obtain an adequate sample, collaboration was sought from consultant psychiatrists in several medical centres within 35 miles of Harrow; collaborators were asked to make a referral to Northwick Park whenever a suitable patient was admitted, i.e. aged between 15 and 70 years, with a first psychotic illness, not unequivocally affective. For the purposes of referral, a "psychotic illness" was defined as one characterised by the presence of delusions or hallucinations occurring in clear consciousness. The clinicians were asked to refer any case that they thought might be suitable and to err on the side of over- rather than under-referral; referred patients remained under their care, and in the hospital to which they had been admitted. They were assessed there by the project psychiatrists (JFM; ECJ; TJC) using Present State Examination (PSE) (Wing *et al*, 1974), Past History and Sociodemographic Schedule (PHSD) (Jablensky *et al*, 1980), Disability Assessment Schedule (DAS) (Jablensky *et al*, 1980), Camberwell Family Interview (CFI) (Vaughn & Leff, 1976) and Disturbed Behaviour Rating (DBR).

The PHSD concerns personal data, the presentation of the illness, and items of personal and family history; it is completed by the interviewer on the basis of an account from an informant as well as the patient. The DAS consists of two sections; one completed by interview of relatives or others who had been living with the patient before admission, and the other by interview with the nursing staff caring for the patient since admission. The first section examines social and occupational functioning before admission and changes in this function over the preceding 12 months. The CFI is used to derive a standardised assessment of emotion and face-to-face contact in the homes of schizophrenic patients; it consists of a semi-structured interview with the relative who spends most time with the patient. This is tape-recorded and later rated according to defined criteria, giving values for Expressed Emotion (EE). Social contact (SC) was derived from a time budget of a typical week.

The DBR was devised by the authors (ECJ and JFM) for use in this project because relatives frequently gave an account of disturbed behaviour during the period when they were seeking the patient's admission, and this behaviour could not be recorded in terms of any of the other assessments.

Not all assessments were completed in every case. The inclusion criteria for a first episode of schizophrenia were applied at the time the assessments were made and were as follows:— age 15–70 years; the presence of a first psychotic episode defined as—no past diagnosis of psychosis or possible psychosis + no previous inpatient care exceeding 3 days + no previous neuroleptic treatment exceeding 3 days (excluding i) outpatient care leading to this first admission and where there was no lapse of care exceeding 30 days (ii) medication with neuroleptic containing preparations advocated for the use of non-psychotic condition (e.g. Motival Motiprès Parstelin); admission to inpatient or day patient care for at least 1 week; a clinical diagnosis of schizophrenia made by the referring clinician; categories C, O or P on PSE: Absence of organic disease with definite or probable aetiological significance.

Sample and findings

A total of 462 patients were referred between 1.8.79 and 2.12.81: 209 cases were excluded and 253 satisfied the inclusion criteria (Table I). The reasons for exclusion are shown in Table I.

TABLE I

Total referred cases		*462*
Age outside range 15–70 years		3
No Present State Examination		64
clinician/patient refused	12	
precipitous discharge	23	
not admitted	9	
not seen	5	
conversation barrier	14	
mental handicap	1	
Clinical diagnosis not confirmed by PSE/Catego		8
probably affective	3	
adolescent behaviour problems	3	
substantial alcohol abuse	2	
Clinical diagnosis not confirmed by PSE/catego		54
D class (depressive psychosis)	22	
M class (manic or mixed affective)	25	
non psychotic classes	7	
Previous episode(s) of psychosis		65
Organic aetiology		15
alcohol abuse/withdrawal	3	
syphilis	3	
drug abuse	2	
sarcoidosis	2	
autoimmune disease	1	
bronchial carcinoma	1	
cerebral cysticerosis	1	
hypothyroidism	1	
head injury/hemiparesis	1	
Total excluded cases		209
First episodes of schizophrenia		253

TABLE II

Social features of 253 first episode schizophrenics

					Total
Racial origin					
White European	166				
West Indian Negro	41				
African Negro	12				=253
Asian	25				
Chinese	1				
Mixed	8				
Mother tongue					
English	208				
Indian (Urdu, Hindi etc)	22				=253
European	14				
Other	9				
Living circumstances					
Alone	104				
with parents	85				
with spouse	41				=253
cohabiting	10				
other relatives	13				
Educational attainments					
None	69				
CSE/O level	48				
HNC/A level	37				=253
HND/1st degree	11				
2nd degree	1				
not known	87				
Social class					
		Peak of career	Most recent	Father	
I/II		21	19	49	
III		90	80	87	
IV/V		52	64	36	=253
Student/Housewife		20	21		
Retired		1	2		
not/known/not applicable (includes unemployed)		69	67	81	

The relatively high number of exclusions is likely to reflect the adopted policy of over- rather than under-referral. The organic illness suffered by 15 patients became evident as more details of the history emerged or as a result of more extensive examination, although a standard programme of physical investigation was not a part of this project. The 253 first episodes of schizophrenia consisted of 148 males and 105 females, of median age 24.9 (range 15–65). Their racial origins, mother tongues, living circumstances, and educational and occupational details are listed in Table II.

Application of the Catego program to the PSE placed 202 cases in S+ class, 29 in P+ class, 8 in P?, 4 in O?, and 6 in D+ (the last were entered during a period when it was not possible to obtain computerised diagnoses).

The informants who assisted in the completion of the PHSD were parents (107 cases), spouses (35 cases), children (five cases), and siblings, other relatives, and associates (17 cases). In 28 cases the patient alone was able to offer information and in 61 it was not possible to attempt the schedule at all because of the patient's incapacity and the lack of a suitable informant. Data concerning medication, admission, and discharge were confirmed by case-note examination.

A history of definite or probable functional psychosis was noted in 12 fathers of patients, 11 mothers, 22 siblings and one child. The nature of the onset of the illness and the events leading to admission were considered in terms of the information on the PHSD, the DAS, and DBR. Onset was graded as acute <5 days (31 patients), subacute 7–30 days (40 patients) and insidious >30 days (93 patients); in 89 patients, either no information was available or it was not possible to grade the onset in these terms. The interval between onset and admission varied considerably and in many cases was surprisingly long: 71 patients were admitted within two months of onset or earlier, 62 at between two and six months following onset, 24 were admitted in the period between six months and one year, in 66 patients, at least one year elapsed before admission, and in 30 the interval could not be ascertained. This interval was frequently a difficult period: social withdrawal, as measured on the DAS, information from the DBR, and the nature and number of contacts made with the helping services were used to assess this difficulty. In the sections of

TABLE III

Disturbed behaviour ratings in 253 first-episode schizophrenics

	Repeatedly	*Once or Twice*	*None at all*	*Ratings unobtainable*
Behaviour potentially threatening to life of patient	14	50	158	31
Behaviour potentially threatening to lives of others	15	33	174	31
Inappropriate or bizarre sexual behaviour	16	21	185	31
Behaviour damaging to property	19	27	176	31
Bizarre or inappropriate not classified above	76	77	69	31

TABLE IV

First-Episode schizophrenia

Numbers of contacts made with various services before contact resulting in admission

	Hospital	*GP*	*Private Medicine*	*Social Workers*	*Religious Bodies*	*Marriage Guidance*	*Other**
No contracts	54	33	176	157	173	185	122
1 contact	86	54	7	15	11	1	41
2 contacts	26	26	0	7	1	1	9
3 contacts	13	25	1	1	2	0	4
4–8 contacts	5	18	0	0	1	0	1
9 or more contacts (ie range 9–33)	6	34	4	9	1	2	12
No information	63	63	65	64	64	64	64
Total contacts	255	566	46	133	33	21	187
Total patients	253	253	253	253	253	253	253

*Includes contacts with all other services such as Mind, self help groups, Citizens Advice Bureaux, employers, embassies, Members of Parliament, but most frequently the police. In 55 cases there was definite police contact which resulted in:
12 patients being detained on Section 60 of the Mental Health Act
11 patients being taken to hospital on Section 136
14 patients being taken to hospital voluntarily by the police
11 patients were charged with offences but later came to admission
7 patients were neither charged, nor admitted nor detained (generally returned to family home).

the DAS completed with the relatives, social withdrawal is rated in six grades; this was completed only where there were informants who had been living with the patients for at least a month before admission, and in 118 cases no assessment could be made. Twenty-five patients showed no dysfunction, 14 minimal social withdrawal, 19 some active avoidance of social interaction, and 24 active avoidance of social interaction and of the presence of others; 28 avoided the presence of others in all circumstances, and 15 were rated as showing maximal dysfunction (for days or weeks, such patients locked themselves in their rooms or wandered aimlessly, making no contact with others and no response to approaches). The abnormal behaviour noted on the disturbed behaviour rating is shown in Table III; 39 patients did not achieve a positive score (i.e. no overt behavioural disturbance described).

The behaviour that these figures represent is not trivial: that threatening to the patient's life includes attempted hanging, actual or attempted self-poisoning, lying on the centre lane of a motorway, etc. Behaviour threatening to the life of others ranges from an ill-organised attempt to hurl an iron bar at a neighbour because of delusions of misidentification, to a prolonged attack occurring over the course of hours, where a patient inflicted multiple wounds with a knife and a walking stick upon his father in the belief that he was the Devil; the father discharged himself from hospital, against medical advice, to arrange the patient's admission. Sexually disturbed behaviour recorded here most frequently refers to explicit behaviour of young men towards their mothers or sisters, and sometimes this was very unusual: one 28 year-old civil servant exposed himself indecently to the wife of a friend, while dressed in a Red Indian suit, and a male postgraduate wearing only a pair of ladies' chiffon knickers walked down the main street of a salubrious suburb, embracing every dustbin that he passed. One especially deteriorated patient walked around his parental home holding his exposed genitals, for weeks.

Behaviour damaging to property ranged from cutting off all of the flower heads in the family garden, through the relatively frequent destruction of the telephone, to the smashing of the entire contents, including furniture, of the family drawing room; other examples included the strangling of a pet budgerigar and the tearing up of £80 in single notes by a patient in impoverished circumstances, who also threw all her shoes in a dustbin. Bizarre and inappropriate behaviour frequently included absence of the patient from home: one patient was returned home from Ireland and Japan, having fled from his supposed persecutors, and other relatives reported return from France, Africa, and nearer to hand, Salvation Army hostels a few miles from home. Incidents in which patients would shout at or otherwise abuse passers-by were commonplace, and behaviour consistent with the belief that the patient was a cat, dog, or more exotic animal was not infrequent.

The nature and number of contacts made with the helping services prior to the contact which led directly to admission are illustrated in Table IV.

Admission was effected by 73 patients after 0, 1, or 2 prior contacts, but in 46 cases, at least nine prior contacts were made with at least one service, before admission was arranged.

The CFI was conducted in 84 cases. It was only considered where the patient had lived with others for three months or longer and was not of an assimilated immigrant background (Macmillan *et al*, pp. 128–133).

Discussion

Within this attempt to examine and document in detail a large sample of patients with first psychotic episodes, 64 (14%) of the referred cases could not be assessed at all; this emphasises the fact that all studies are limited to patients who are relatively willing or able to cooperate, and that participants are likely to be, to some extent, unrepresentative of the sample from which they are drawn. As the number and complexity of assessments increased, the percentage of patients in whom complete data could be obtained became less: assessments which depended upon an informant could not be used in the 41% of the first schizophrenic episode cases who lived alone, while the unassimilated immigrant background of some patients limited the use of some assessments, particularly the CFI.

The occurrence of psychoses clinically indistinguishable from schizophrenia in association with various organic pathologies has been well described (Davison & Bagley, 1969), and in this study, 15 organically ill cases were found who at the point of referral were considered to have schizophrenia, and where initial presentation was considered by the project psychiatrists to be consistent with that clinical diagnosis. This frequency is little different from that recorded by McClelland *et al* (1966), and by Small *et al* (1966). Although the extent of physical investigation was variable, the patients were, where possible, followed-up for up to two years, and further organic disease did not become apparent during that time. Thus, although it is possible that relevant organic pathology was overlooked, this is unlikely to have been frequent. The statement "The vast majority of patients displaying a schizophrenic syndrome have no detectable organic disease (Davison & Bagley, 1969)" remains true. Among the 253 cases who satisfied the study criteria for first schizophrenia episodes, females were older than males at admission. (median F 26.7; M 24.1; $Z=1.47$ $P=0.14$, Mann Whitney) and at onset (median F 24.8; M 23.0; $Z=1.59$; $P=0.11$, Mann Whitney). This is in keeping with previous work (Lewine, 1981).

In his early descriptions, Kraepelin (1919) noted that while in some cases of *dementia praecox*, the onset is acute and takes place over a matter of a few days, in others it is gradual and insidious. The variability of onset found in the present study is thus to be expected. The long duration of the interval between onset and admission in many cases was perhaps more surprising, although delay between onset and admission in excess of one year has been reported (Achte, 1967; Nyman & Jonsson, 1983). The reasons for the delay are not easy to determine: the available information was from the patients and relatives, and we have no account from the general practitioners, social workers, or psychiatrists who were involved. While there is evidence (e.g. Marx *et al*, 1973) that serious mental illness can, in some cases, be managed without admission, all patients in this study came to inpatient care, and there is no reason to think that this followed a planned attempt at outpatient management which proved inadequate. The situation described by many relatives was of difficulty in obtaining appropriate assessment and in arranging adequate management. The difficulties in making the diagnosis in some cases of early schizophrenia have been well documented (Gillies, 1958), and clearly it is unwise prematurely to leap to a diagnosis of psychotic illness. It is perhaps unrealistic to hope that admission can always be arranged after no more than three contacts, as it was in 73 of the present cases. On the other hand, the fact is regrettable that in 46 cases, at least nine contacts were made before that which led directly to admissions; whatever the diagnostic difficulties may have been, the needs of a substantial proportion were not met.

The contacts that the relatives made in general were appropriate, in that they sought medical aid, while the more unusual contacts listed under "other" were made by relatives who had failed to obtain the assistance that they sought from more orthodox sources. Though relatives were often distressed by the necessity for police contact, in many instances they sought it and were frequently grateful for the ready admission that followed, although there were two notable exceptions to this.

This study underlines the very severe disturbance associated with schizophrenia, in terms both of positive disturbed behaviour and social withdrawal.

Although difficult to define objectively, both the concern and tolerance of relatives impressed the authors; by the relatives' account, the patient whose assessment and admission had gone smoothly was exceptional. Even if allowance is made for the possibility that in their distress the relatives might be unduly sensitive to defects in the psychiatric services, the facts concerning disturbed behaviour and number of contacts made allow no interpretation other than that appropriate services were not available to these people when they were required. To some extent, this may have been due to the fact that these relatives had not previously had occasion to deal with the psychiatric services: in particular, knowledge of the availability of domicillary consultations for patients who refused to visit doctors or hospitals was not widespread, and several difficult situations could have been avoided had the relatives known that they themselves could make application for the patient's admission under the Mental Health Act. Some general practitioners and social workers were uncertain of the appropriate courses of action when the patient refused interview. The management of a first psychotic episode will not be a frequent occurrence for either general practitioner or social worker, and it appeared that in some instances, adequate advice and support from the psychiatric services was not sought or was not available. Some relatives made repeated contacts with non-medical services (Table IV), and for them, the availability of an emergency walk-in clinic would have provided a stop-gap for the evident deficiencies in the service (Bennett *et al*, 1972).

While these difficulties may in part be due to the nature of the patients' condition, the distress of their relatives, and the inexperience of GPs and social workers in this situation, these findings must cause serious disquiet to psychiatrists and others responsible for the services.

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II. A Randomised Controlled Trial of Prophylactic Neuroleptic Treatment

T. J. CROW, J. F. MacMILLAN, A. L. JOHNSON AND E. C. JOHNSTONE

Out of 253 patients fulfilling criteria for a first episode of schizophrenic illness, 120 entered a randomised placebo-controlled trial of maintenance neuroleptic medication on discharge; they were followed to relapse or loss to follow-up, for two years or to the end of the study. Of those on active medication, 46% relapsed, as did 62% of those on placebo; the most important determinant of relapse was duration of illness prior to starting neuroleptic medication. This finding might be because extended duration of symptoms before admission is more likely to be present in illnesses which in any case will have poor prognosis, or because susceptibility to relapse is reduced by early institution of treatment. The study provides no data on which a decision between these alternative explanations can be based.

While neuroleptic treatment in schizophrenia is effective in preventing relapse (Davis, 1975), most clinical trials (eg Leff & Wing, 1971; Hogarty *et al*, 1974) indicate that a number of patients do not relapse, even though they receive placebo. Nearly all trials have included patients who had suffered more than one psychotic episode, so that it is possible that following a first schizophrenic illness, the proportion of patients who will do well without treatment is higher than the 15 to 20% in these trials who remained well on placebo after one to two years. There have been some claims to this effect. On the basis of his own follow-up studies, M. Bleuler (1978a & b) has asserted that "at least 25% of all schizophrenics recover entirely and remain recovered for good", even though they do not receive long-term neuroleptic medication, but Bleuler's criteria for recovery however allow the persistence of delusions and perceptual disturbance.

Since neuroleptic drugs have undesirable effects, and patients are often reluctant to take them, it is important to ascertain the characteristics of the population who will or will not benefit from long-term medication. Little systematic information about this has been collected, though Simpson & May (1982) suggest that "patients asymptomatic after first episodes of treatment may normally be tapered off drugs within six months" but offer no evidence in support of this strategy. May *et al* (1981) examined the effects of five treatment regimes in 228 first-admission schizophrenics and followed the sample for five years, but treatment in the post-discharge phase was not examined as an independent variable. Kane *et al* (1982) found an advantage of ($P<0.01$) for depot fluphenazine in preventing relapse in a group of 28 patients with first episodes of schizophrenic illness; no prognostic factors were identified, and the beneficial effects of medication did not reach statistical significance in the 21 patients who met RDC (Spitzer *et al*, 1977) criteria for schizophrenia.

The present study was designed to compare the policies of active and placebo neuroleptic medication respectively in preventing relapse following a first schizophrenic illness (defined by PSE criteria) and to identify the clinical features which predict response to such medication. Since previous studies (eg Hogarty *et al*, 1974) indicated that more than 50% of schizophrenic patients are likely to relapse in a two-year period, a satisfactory study would require at least 100 patients, and preferably more (Peto *et al*, 1976). Since it was estimated that a psychiatrist working in the UK National Health Service with a catchment area population of 50,000 may see between eight and ten patients suffering from first schizophrenic illnesses in one year, the trial required the participation of psychiatrists from several centres.

Methods

Patient selection

Psychiatrists working in both psychiatric and district general hospitals (Table I) accessible from Northwick Park Hospital were asked to participate. In each hospital some consultants, but not others, took part. For this reason, the population from which the trial sample was drawn cannot be specified with precision, but it includes the predominantly urban and suburban practices of a broad range of general adult psychiatrists.

Participating psychiatrists were asked to refer all patients aged 15 to 70 years admitted to inpatient or day patient care who were suffering from a first psychotic episode which was not unequivocally affective (see Johnstone *et al*, 1985 Table I). After referral, the patients were assessed in hospital by a project psychiatrist (JFM, ECJ, TJC).

Inpatient care

Management of the initial episode was at the discretion of the clinician responsible for the patient. Contact with the patients' progress was maintained by the project psychiatrists, and when discharge was envisaged, consent to the trial was sought from the clinician, the patient, and the relatives. The patient's clinician was then asked to prescribe one (and one only) of the following five neuroleptics, at or above the stated minimum dose (no upper limit):

Flupenthixol	IM	40 mg/month
Chlorpromazine	Oral	200 mg/day
Haloperidol	Oral	3 mg/day
Pimozide	Oral	4 mg/day
Trifluoperazine	Oral	5 mg/day

Other psychotropic (but not other neuroleptic) medication could be prescribed in addition, as thought necessary; once a neuroleptic had been prescribed, it was intended to maintain the patient on that drug throughout the period of participation.

The index episode was considered to have come to an end when the patient was discharged from full or partial (including day) hospital care and had maintained such discharged status for 30 days or more. Where readmission took place within 30 days, this was considered an extension of the index episode. Outpatient care was conducted by the clinical teams at each hospital, and the use of hostels, rehabilitative centres, and day attendance at facilities in the community were arranged as appropriate.

Randomisation and supply of trial medication

Randomisation and trial medication was arranged by the Pharmacy Department in Northwick Park Hospital. Using allocation lists prepared for each of the five drugs above, patients were randomised to receive active or placebo medication. The research team, the clinician responsible for the patient, and the patient remained blind to the nature of the medication. For the first month following discharge, all patients received active drug. Those who had been allocated active treatment remained on active drug thereafter; those allocated placebo were tailed into placebo treatment, receiving half-strength matched medication during the second month and matched placebo thereafter. This procedure was adopted to avoid withdrawing active medication suddenly at discharge, which is a time of stress, and to maintain the blindness of the study. The patient's neuroleptic (or placebo) dosage could be changed at any time, at the clinician's discretion, but was not allowed to fall below the stated minimum dose.

Care following discharge

Clinicians were asked to review and rate their participating patients at least once a month for the first six months of follow-up and six-weekly thereafter, up to two years from randomisation. Delusions and hallucinations were rated as present, absent, or doubtful and any other clinical features were noted, as well as the dosage of neuroleptic and additional drugs. The main outcome variable of this study was relapse ascertained by the responsible clinician, who notified the trial centre when it occurred. Because this was a placebo-controlled study, clinicians were encouraged to manage relapse with readmission wherever possible. Relapse was defined as readmission to psychiatric care for any reason; readmission considered necessary by the clinicians responsible for the patient but for some reason (eg lack of beds, refusal of patient) not possible; active antipsychotic medication considered by the responsible clinician to have become essential because of features of imminent relapse. On relapse, the trial treatment (active or placebo) was revealed to the responsible clinician, who continued treatment as considered appropriate.

Statistical analysis

For each patient the period from randomisation to either relapse, loss to follow-up, follow-up for two years or until 1st August 1982 (whichever was the earlier) was calculated to the nearest week. Actuarial percentages relapse-free at weekly intervals from the first trial prescription were calculated for the active and placebo-treated groups, as well as for other sub-divisions of the data. The resulting percentage relapse-free curves have been compared, using the logrank test (Peto *et al*, 1977). The difference between the two treatment groups was adjusted for baseline variables considered to be of prognostic importance.

Results

From 1.8.79 to 2.2.82, when recruitment ceased, 120 patients were entered in the trial; follow-up terminated on 1.8.82.

TABLE I
Distributions by treatment on baseline variables

	Active	*Placebo*	*Total*
Sex			
Male	35	39	74
Female	19	27	46
Centre			
Northwick Park	15	17	32
Luton and Dunstable	15	18	33
Shenley and Wembley	10	16	26
Hill End	3	4	7
St. Bernard's and St. John's	1	2	3
St. Mary's	3	5	8
Napsbury	2	1	3
Friern, Royal Free, Whittington and Chase Farm	5	3	8
Ethnic origin			
White European	38	45	83
West Indian Negro	7	9	16
African Negro	2	1	3
Asian	6	8	14
Chinese/Oriental	—	1	1
Mixed	1	2	3
Mother tongue			
English	41	54	95
European	5	3	8
Oriental	—	1	1
Indian	6	6	12
Other	2	2	4

TABLE I (*Continued*)

	Active	*Placebo*	*Total*
Period between onset of illness and hospital admission (months)			
<1	11	16	27
1–2	6	9	15
2–6	9	22	31
6–12	7	6	13
12–24	11	5	16
24–48	6	1	7
48–	3	5	8
NK	1	2	3
Median (range)	5.7 (> 1–101)	2.4 (< 1–92)	2.8 (< 1–101)
Period between hospital admission and discharge (weeks)			
<2	—	3	3
2–3	4	4	8
3–4	1	24	25
4–8	19	24	43
8–12	14	7	21
12–	16	25	41
Median (Range)	8.5 (2–74)	8.0 (1.5–40)	8.2 (1.5–74)
Age at randomisation (years)			
15–19	7	7	14
20–24	12	28	40
25–29	9	11	20
30–39	12	15	27
40–49	10	3	13
50–59	4	2	6
Mean (Range)	28.2 (17–59)	24.3 (16–56)	26.3 (16–59)
Year of randomisation			
1979	4	8	12
1980	31	33	64
1981	18	25	43
1982	1	—	1
Present State Examination			
S+	41	53	94
P+	10	7	17
P?	—	2	2
O+	—	1	1
D+	3	3	6
Discharge drug			
Chlorpromazine	3	5	8
Depixol	31	32	63
Haloperidol	3	6	9
Pimozide	5	8	13
Trifluoperazine	12	15	27
Place of discharge			
Home	49	63	112
Hostel	5	3	8
Return to work			
Employment	23	20	43
Unemployment	29	43	72
Day Centre	2	1	3
student	—	1	1
Not known	—	1	1
TOTAL	54	66	120

Index episode

All patients were treated as inpatients, although the duration varied widely (see Table 1), and with neuroleptic drugs of varying nature and dosage. One received ECT and one was also given lithium; hypnotics, anticholinergics, and tricyclics were also prescribed. The distributions of patients' demographic and clinical variables are shown for each treatment group in Table I.

Comparison of the distribution of patients on the two trial treatments (active and placebo) suggests imbalances in the period between onset and admission ($X^2=8.41$, df=5, $P=0.14$), the period between admission and discharge ($X^2=5.41$, df=3, $P=0.14$), and age at randomisation ($X^2=10.1$, df=4, $P=0.039$). Patients given active drugs had longer periods between onset of illness and admission, spent more time in hospital, and were older than patients given placebo.

Relapse

The status of all patients at the conclusion of the trial is shown in Table II, together with the actuarial percentages relapse-free at six-month intervals from trial entry (standard errors are given where the number of patients at risk exceeds ten).

In 13 cases, follow-up was incomplete, as contact with the patients could not be re-established. The reasons were: six declined further contact, five left the area, one became pregnant and was withdrawn, and the remaining patient was withdrawn by her general practitioner. None had relapsed when contact was lost.

Although relapse was determined by the responsible clinician, the trial psychiatrists visited the patients, and categorised the relapses as:

> development of psychotic features noted at interview by clinician (active 23; placebo 36); behaviour indicative of deterioration described by relatives or others (active 1; placebo 2); deterioration of mental state without development of psychotic features noted by clinician (active 1; placebo 1); death from drowning in the bath for which the coroner recorded an open verdict (placebo 1), and an uncharacteristic non-cooperation (placebo 1).

Within the follow-up period, 25 (46%) of patients on active medication experienced relapse, compared with 41 (62%) of patients on placebo. Although the mental state ratings during the follow-up period were not used for the calculation of the results, which were based upon the clinician's decision of relapse/relapse-free, these ratings generally confirmed that the patients who had relapsed were psychotic and those who were relapse-free were well. At the point of entry to the trial 91 patients were rated as well, 13 were noted to have psychotic features, 10 to have a defect state and 6 were said to have non-specific symptoms. At the point of relapse the ratings showed 58 patients to have psychotic features and none to have a defect state. One patient was dead, one had attempted suicide, one was depressed, one had a toxic confusional state, in 3 there was

TABLE II
Status of patients at conclusion of trial⁺

Treatment group	*Entered in trial*	*Relapse-free*		*Relapsed*	*Actuarial % relapse-free (standard error** at (months)*			
		Complete follow-up	*Incomplete follow-up*		*6*	*12*	*18*	*24*
Period between onset and first trial prescription < 1 year								
Active	31	18	3	10	80 (7)	80 (7)	71 (9)	59
Placebo	51	18	7	26	66 (7)	45 (8)	42 (8)	42
Sub total	82	36	10	36	72 (5)	59 (6)	54 (6)	48 (6)
Period between onset and first trial prescription > 1 year								
Active	22	5	2	15	76 (9)	33	26	18
Placebo	13	0	0	13	23	8	—	—
Sub-total	35	5	2	28	55 (9)	23	14	10
Period not known								
Active	1	0	1	0	—	—	—	
Placebo	2	0	0	2				
Sub-total	3	0	1	2	—	—	—	—
All patients								
Active	54	23	6	25	79 (6)	62 (7)	54 (7)	42 (8)
Placebo	66	18	7	41	57 (6)	37 (6)	33 (6)	30
TOTAL	120	41	13	66	67 (4)	48 (5)	42 (5)	35 (5)

**Standard errors given when a number of patients at risk exceeds ten
⁺Either 2 years from randomisation or 01.08.82 whichever earlier

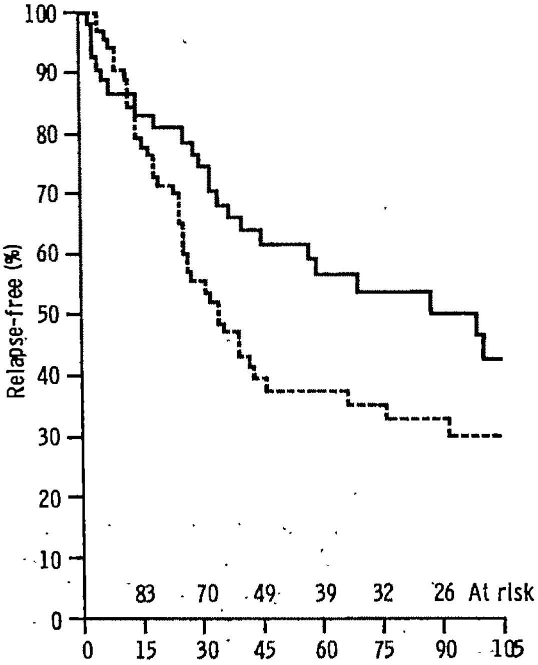


FIG. 1 Actuarial percentage relapse-free curves for patients on active (——, 54 patients) and placebo (- - -, 66 patients).

a report of disturbed behaviour and one showed uncharacteristic non-cooperation. In those who were relapse free at 2 years, closure of the trial or loss to contact the final ratings recorded 46 patients as well, four with psychotic features and three with a defect state. The remaining patient was pregnant but evidently otherwise well.

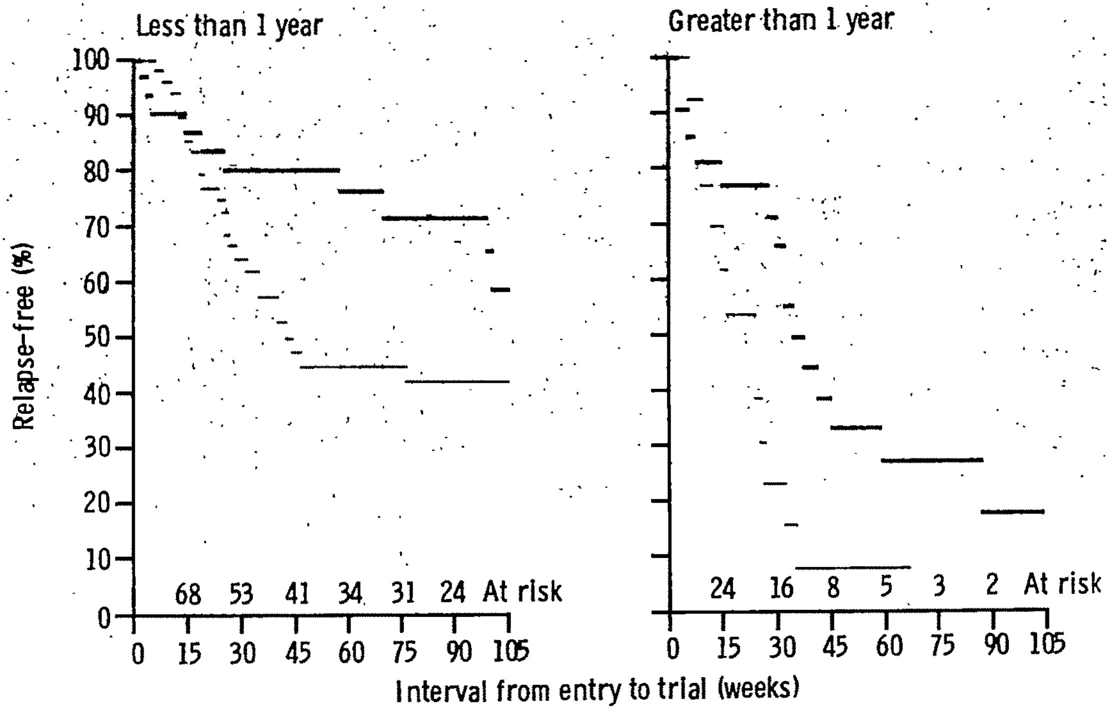
Actuarial percentage relapse-free curves for active- and placebo-treated groups are shown in Figure 1; comparison of these curves with patients stratified by the period between onset of the index episode and hospital admission (< 1 year and at least 1 year) indicated that the relapse rate was higher in placebo-treated than in active-treated patients (Figure 1) (X^2: 9.40, df = 1, $P = 0.002$).

Determinants of relapse

An objective was to define those clinical features which predict response to neuroleptic maintenance therapy. Since such prediction is reliable only with a very large sample, the results for the present 120 patients should be interpreted cautiously.

(a) Nature of drug prescribed

Sixty-three cases were prescribed flupenthixol (31 active, mean dose 83.5 mg/month; range 40–400 mg/mth; 32 placebo, mean dose 85.9 mg/month; range 40–400 mg/month), eight chlorpromazine (three active, mean dose 366 mg/day; range 200–600 mg/day; five placebo, mean dose 250 mg/day; range 200–300 mg/day), nine haloperidol (three active, mean dose 11.75 mg/day;


Less than 1 year

Greater than 1 year

FIG. 2 Actuarial percentage of patients relapse-free subdivided by period between onset and first trial prescription and by treatment (——active); (———placebo).

range 6–19.5 mg/day; six placebo, mean dose 10.5 mg/day; range 3–21 mg/day), 13 pimozide (five active mean dose 7.75 mg/day, range 4–16 mg/day, eight placebo, mean dose 5.5 mg/day, range 4–12 mg/day), and 27 trifuoperazine (12 active mean dose 11.5 mg/day, range 5–20 mg/day; 15 placebo mean dose 13.9 mg/day range 5–45 mg/day). Thus, the range of dosages used did not differ substantially between active- and placebo-treated patients, nor did the use of other psychotropic medication (antiparkinsonian agents prescribed for 32 active cases and 32 placebo cases; antidepressant for six active and two placebo cases and anxiolytics for 11 active and 12 placebo cases). There were too few patients on each neuroleptic to allow a comparison of the separate treatments.

(b) Age, sex, ethnic origin

Age at randomisation was not related to relapse, nor was the year of randomisation. Sex, ethnic origin, and mother tongue were not related to relapse. The small numbers of patients at some of the treatment centres precluded meaningful comparison between centres.

(c) Temporal factors

The time between admission and first trial prescription indicates the duration of inpatient/day-patient care; it was not related to relapse. The time between the onset of illness and first trial prescription was, however, a major determinant of relapse. Relapse was commoner ($P<0.0001$) in patients for whom this interval was greater than one year than in those for whom it was less (Table II, Figure 2).

There is an imbalance in the distribution of the patients in active and placebo groups for this variable and the comparisons of treatment groups take this into account (Table I).

(d) Clinical and social variables

The 94 patients in the S+ major class category on PSE were compared with the remainder, and this comparison was not relevant to relapse. Place of discharge (home or hostel) did not affect relapse, but return to work was associated with a lower relapse rate than the other occupational categories ($X^2=14.6$, $df=1$, $P=0.0001$). The fact of returning to work is, of course, likely to be associated with features such as relatively complete recovery or previous work record which relate to progress (Cooper, 1961).

Deviations from protocol

Six patients entered the trial at a time at which computerised classification of the PSE was unavailable, and were later found to be in Category D+; they continued in the study.

Seven patients changed their prescribed trial drug (four from flupenthixol to pimozide, one from flupenthixol to trifluoperazine; one from haloperidol to flupenthixol; one from trifluoperazine to pimozide). Allocation to active drug or placebo was unchanged.

Discussion

The relapse rates in this study (58% on active medication and 70% on placebo within two years of discharge) are high, and apparently greater than those in the 28 patients with first episodes observed by Kane *et al* (1982), of whom 41% on placebo and none on neuroleptic medication relapsed within one year. In that study, patients in whom poor compliance was anticipated were placed on depot medication; in the present one, choice of neuroleptic was in the hands of the responsible clinician, and more than half the patients were treated with depot medication. There were no differences in relapse rates between depot and oral medication; some previous studies (e.g. Falloon *et al*, 1978) have shown no difference in relapse rates between patients treated with oral and depot prophylactic neuroleptics following schizophrenic episodes, and Hogarty *et al* (1979) concluded that the high rate of schizophrenic relapse is not adequately explained by poor compliance.

The definition of relapse is arbitrary (see Falloon *et al*, 1978). Because this study was a multi-centre one and the decision that relapse had occurred or was imminent rested with a large number of collaborating clinicians, a wide interpretation was appropriate, and this may have contributed to the high relapse rates. Nonetheless, in 59 of 66 relapses, the clinician noted that psychotic features had developed.

This study confirms in patients with first schizophrenic episodes the benefits of neuroleptic medication which have been demonstrated for schizophrenics in general. With period between onset of the index episode and hospital admission taken into account, the effect of medication is significant ($P=0.002$). In spite of the difference between this sample and that studied by Hogarty *et al* (1974), comparison of the percentage rates in the two trials is instructive:

	2-year relapse rates (%)	
	Active	*Placebo*
Hogarty *et al* (1974)—unselected	48	80
Present study—first episodes	58	70
95% confidence limits	(42.74)	(58.82)

These figures are not adjusted for the period between onset and admission, but Hogarty's estimates are within the 95% confidence of our two-year relapse rates. In both studies, a proportion of patients remained relapse-free without neuroleptic medication at the end of the follow-up period, but the relapse rate (65%) remained high. May *et al* (1981) concluded from their three to five-year study of first episode schizophrenic patients that "overall, the follow-up outcome is far from reassuring, whatever the type of treatment." First episodes of schizophrenia are harbingers of late episodes; some patients avoid further episodes without medication, but the two-year assessment suggests that the proportion is less than 30%. The figure of 30% does not take account of 17 patients eligible for entry who did not achieve discharge before termination of recruitment. A further proportion of the sample will relapse later, and others will retain stigmata of psychosis of lesser degree than those requiring hospital readmission. The proportion of the original sample in which Bleuler's 25% who "recover entirely and remain recovered for good" must be found is perilously depleted by two years.

The attempt to define predictors of outcome and response to medication isolated a variable of substantial effect—period between onset of symptoms and admission to hospital. The outcome in patients in whom this interval exceeded one year is particularly striking (Table II, Figure 2); all patients given placebo have relapsed at two years, and only 18% given active treatment are relapse-free. In this subgroup, outcome is thus worse than in patients unselected by stage of illness (eg, in the trial sample of Hogarty *et al,* 1974): possible reasons for this poor outcome deserve consideration. One possibility is that some feature associated with high risk of relapse leads to delay in admission: a slow and insidious onset might lead to later admission, and might be independently associated with poor outcome. Similarly, lack of social support (itself perhaps related to insidious onset) could delay hospital admission, but also be related to earlier relapse after discharge. A second, perhaps more arresting explanation is that delay in institution of treatment itself leads to poorer long-term outcome, *i.e.* that persistence of symptoms untreated by neuroleptic drugs leads to abnormality, which cannot be completely reversed by subsequent treatment; such a possibility should not be too readily dismissed. Few trials have yielded pertinent information, but the study of May *et al* (1981) is relevant, its trial phase was confined to the period of the patient's first hospital admission, treatment subsequent to discharge being outside the investigator's control. Nevertheless, patients treated with neuroleptic drugs in the trial phase did much better in terms of outcome in the subsequent three years, and the group treated initially without drugs, who spent a longer time in hospital in the trial phase, did worse. These findings, therefore, are consistent with the possibility that drug treatment in an active phase of the illness has enduring effects.

The view that early institution and continuation of neuroleptic medication determines longer-term outcome in schizophrenia contradicts some recent opinions. Carpenter *et al* (1977) argued that some patients will do well without drugs, even in the psychotic phase, and considered the possibility that drugs may actually enhance the risk of later relapse. Rappaport *et al* (1978) claimed that patients treated without medication whilst in hospital did better at follow-up than patients treated with chlorpromazine. However, there are methodological flaws in both studies, as treatment trials. As Carpenter *et al* (1977) point out, their study was not based on random allocation, and drug treatment was in fact administered to some patients in a group intended to be drug-free. Rappaport *et al* randomly allocated patients to placebo or medication in hospital, but the critical comparisons were made after a follow-up phase in which medication was not controlled. Neither study provides compelling evidence that there are groups of patients with schizophrenia in whom the avoidance of medication at particular phases of the illness has significant advantages. Our study also has failed to identify a group of patients who will do well without drugs after a first episode of psychosis.

We conclude that prophylactic benefits of neuroleptic medication in schizophrenia have been amply demonstrated by previous work, and that no sub-group of patients has been identified, either in previous studies or in the present sample of first episodes of illness, who can be recommended to discontinue medication without incurring an increased risk of relapse. Whether or not there is a point in time at which medication can safely be discontinued, has not been established (Hogarty & Ulrich, 1977), nor has the minimal effective dose been ascertained, although recent trials (Branchey *et al,* 1981) have considered this problem.

However, the new issue raised by this study is whether medication instituted early and continued during and perhaps after an acute episode of illness will have enduring beneficial effects on the course of the condition. One, but not the only interpretation of our findings is that the failure to institute early treatment is associated with the development of a high susceptibility to relapse. It has been established (Johnstone *et al,* 1985) in the population from which the sample was drawn, delays in diagnosis and admission to specialist care were common and often prolonged. Further study of the effects early institution of treatment is required, since to date, only the work of May *et al* (1981) provides information relevant to this question.

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III. Short-term Outcome in Trial Entrants and Trial Eligible Patients

J. F. MacMILLAN, T. J. CROW, A. L. JOHNSON AND E. C JOHNSTONE

Of 253 patients from nine medical centres identified with first episodes of schizophrenic illness, 17 did not achieve discharge during the period of trial recruitment. 120 entered a randomised controlled trial of neuroleptic medication and were followed-up, as were 116 who were eligible for the trial but did not enter it. Overall, 60% of the sample had relapsed within two years of discharge; age, sex, ethnic origin, duration of admission, social withdrawal before admission, and type of onset of illness were not significantly related to relapse. Relapse rates were lower on active trial or standard medication than placebo, but however assessed, outcome at this early stage was poor for many patients.

The many studies of the outcome of schizophrenic episodes (Stephens, 1978) include some with over 400 patients, eg Astrup *et al* (1962); Huber *et al* (1975) and several with follow-up periods of five and ten years (Stephens, 1978). A few examined the outcome after 30, 40 or even 50 years (Tsuang & Winokur, 1975; Vaillant, 1963). This study described follow-up to two years from discharge of 253 patients who participated in a multi-centre study of first schizophrenic episodes (Johnstone *et al*, Crow *et al*, 1985). While the size and duration of follow-up of this study are unremarkable, it is unusual in including only first episodes; previous such studies have been retrospective. Lindelius (1970) studied first-episode schizophrenics admitted between 1900 and 1901, and therefore inaccessible to personal interview, Cooper (1961) 237 patients discharged following first episodes between 1953 and 1957, of whom only 35 were interviewed, and Nyman & Jonsson (1983) patients six to nine years after admission (not interviewed by the investigators, and information obtained from the case notes and a questionnaire). The opportunity to examine outcome in a sample of first-episode schizophrenic patients who were documented and followed-up by the investigators is therefore unusual and its interest is enhanced by the widely differing circumstances of the patients, and by a range of treatment policies in nine different centres. The study also offers the opportunity of comparing outcome in a group of schizophrenic patients who entered a study and in those who did not, since approximately half the sample entered a controlled clinical trial, whilst the remainder received standard care.

Method

The 253 patients in this study were selected from a total sample of 462 patients with apparent non-affective first psychotic episodes, referred from nine medical centres (Johnstone *et al*, 1985). Detailed assessments, in part derived from the WHO studies of schizophrenia (Jablensky *et al*, 1980), were conducted on all 462 patients until they failed on one of the eligibility criteria for entry to a clinical trial (Johnstone *et al*, 1985). The 253 patients who satisfied all these criteria were followed-up for a maximum of two years, and comprise three groups:

(a) Clinical trial entrants: 120 (Crow *et al*, 1985).

(b) Trial-eligible patients: 116 patients, these achieved discharge but were not included in the drug trial because of refusal (patient/relative 43, clinician 22) precipitous discharge (21), unsuitable medication (15), emigration/departure from area (10), or multiple reasons (5).

(c) Non-discharged patients: 17.

The trial entrants attended for follow-up monthly or six-weekly for two years or until relapse, loss of contact, or the close of the study, whichever was earliest (Crow *et al*, 1985). Relapse was frequently, but not invariably followed shortly by readmission. For the trial-eligible patients, information about outcome was gleaned by personal contact and/or case note perusal at the close of the study. Particular note was taken of readmission, since this was considered to be the best available parallel to relapse in the trial entrants.

Statistics

Comparisons between the groups for distribution on baseline variables have been made using the chi-squared test; comparisons of relapse times have been made using the logrank statistic (Peto *et al*, 1976, 1977). Specifically, the period from discharge to relapse, close of the study (two years follow-up or 1st August 1982), or loss to follow-up, whichever was the earliest, was calculated to the nearest week for each patient. Actuarial relapse-free curves were calculated, using the life-table method, at weekly intervals of follow-up for both trial patients (sub-divided by treatment active or placebo) and trial-eligible patients. In assessing prognostic factors patients in the trial allocated active treatment and trial-eligible patients have been combined in a single group.

Results

The 253 patients consisted of 120 trial entrants, 116 trial-eligible patients, and 17 who were never well enough to be discharged. The distributions of patients on socio-demographic variables are shown in Table I.

The groups of trial and trial-eligible patients are essentially similar, except that the period between onset of illness and hospital admission is shorter for the trial entrants ($X^2 = 10.4$, $df = 5$, $P = 0.065$), and more of the trial-eligible patients than of the trial entrants are hospitalised for less

TABLE I
Distribution of patients on socio-demographic variables

Variable	*Classification*	*Trial entrant*	*Trial eligible*	*Not discharged*	*Total*
Sex	Male	74	65	9	148
	Female	46	51	8	105
Race	White European	83	70	13	166
	West Indian Negro	16	22	3	41
	African Negro	3	9	1	13
	Asian	14	11	—	25
	Chinese	1	—	—	1
	Mixed	3	4	—	7
Mother Tongue	English	95	97	15	207
	Romance	8	5	2	15
	Indian (Hindi etc)	12	10	—	22
	Chinese (Mandarin)	1	—	—	1
	Other	4	4	—	8
Year of admission	1979	28	17	2	47
	1980	59	51	2	112
	1981	33	48	13	94
Age at admission	15–19	15	16	2	33
	20–29	59	63	9	131
	30–39	28	19	5	52
	40–49	12	13	1	26
	50–59	6	4	—	10
	60–65	—	1	—	1
	Median (range)	25·3 (16–59)	24·8 (15–65)	23·3 (18–46)	24·9 (15–65)
PSE major class	S+	94	95	12	201
	P+	17	8	4	29
	P?	2	6	—	8
	O+	1	1	1	3
	O+	—	5	—	5
	D	6	—	—	6
	NK	—	1	—	1
Period between onset and admission	<4 weeks	28	24	1	53
	5–8 weeks	17	4	1	22
	9–26 weeks	31	29	2	62
	27–52 weeks	10	9	1	20
	1–2 years	16	6	2	24
	>2 years	15	19	8	42
	Not known	3	25	2	30
	Median (wks) (range)	16 (<1–440)	18 (<1–830)	111 (4–490)	18 (<1–830)

TABLE I (*continued*)

Variable	*Classification*	*Trial entrant*	*Trial eligible*	*Not discharged*	*Total*
Period between admission & discharge	<2 weeks	3	11		14
	2–4 weeks	12	21		33
	5–8 weeks	43	24		67
	9–26 weeks	51	47		98
	27–52 weeks	10	10		20
	1 year	1	3		4
	Median (wks) (range)	8 (1·5–76)	8·5 (0·5–81)		8 (0·5–81)
Period between onset & discharge	<8 weeks	15	12		27
	9–26 weeks	36	21		57
	27–52 weeks	30	25		55
	1–2 years	20	13		33
	>2 years	16	20		36
	Not known	3	25		28
	Median (wks) (range)	29 (2–440)	33 (4–850)		31 (2–850)
Place of discharge	Home	112	102		214
	Hostel	8	6		14
	Not known	0	8		8
Employment on discharge	Employed	43	13		56
	Unemployed	72	72		144
	Day centre	3	12		15
	Student/HW/NK	2	19		21
	TOTAL	120	116	17	253

than four weeks ($X^2 = 12.7$, df = 4, $P = 0.013$), although the median hospitalisation times of the two groups are similar. A higher proportion of trial entrants had returned to employment ($X^2 = 14.7$, df = 1, $P < 0.001$).

Hospital career

To account for patients seeking early discharge only to be rapidly readmitted, the index admission was considered to be concluded when the patient remained out of hospital for 30 days. The status of all discharged patients at the conclusion of the study and actuarial percentages relapse/readmission free at six-monthly intervals for the two-year duration of the study are shown in Table II. Four of the 253 patients (one trial, one trial-eligible, one non-discharged, and one former trial patient) are known to have died, from drowning (one case), from overdose and/or suffocation (3 cases). Two verdicts of suicide, one of misadventure, and one open verdict were returned.

Since both the period between onset of illness and discharge, and treatment were shown to be major determinants of relapse (Crow *et al*, 1985), these factors have been incorporated in Table II. Actuarial percentage relapse-free curves are illustrated in Figure 1.

Overall, about 60% of patients with first schizophrenic episodes relapse within two years of discharge. There is a difference in relapse rates between the combined active treatment and trial-eligible patients and placebo treatment (adjusted for period between onset of illness and discharge, logrank statistic $X^2 = 10.0$, df = 1, $P = 0.0016$). Determinants of relapse/readmission in terms of socio-demographic and clinical variables were sought in the 236 discharged patients. The differences in treatment in terms of the prescription of placebo, active, and standard medication were taken into account. Age ($X^2 = 0.50$, df = 2, $P = 0{\cdot}78$), sex ($X^2 = 0.41$, df = 1, $P = 0.52$), ethnic origin ($X^2 = 1.36$, df = 2, $P = 0.51$), mother tongue ($X^2 = 0.82$, df = 1, $P = 0.36$), and duration of admission ($X^2 = 3.03$, df = 2, $P = 0.22$) were not related to relapse.

Those returning to employment were significantly less likely to relapse ($X^2 = 14.6$, df = 1, $P < 0.01$) and those returning to a hostel significantly more likely to do so than those returning home ($X^2 = 4.16$, df = 1, $P = 0.041$). The number of patients in some PSE categories (Wing *et al*, 1974) were too small for individual comparisons, but when all the S+ class was compared with the remainder in terms of relapse/readmission, no difference was found ($X^2 = 0.73$, df = 1, $P = 0.39$). Items from the Past History and Socio-Demographic Schedule and Disability Assessment Schedule (Jablensky *et al*, 1980) which to some extent, corresponded with the predictive prognostic factors of duration of onset, premorbid personality, and domestic adjustment described previously (Schofield *et al*, 1954; Valliant, 1962) were considered as possible determinants of relapse. These were social withdrawal, change in social withdrawal over the past year, type of onset (<7 days; >7 days and <1 month: >1 month), past occupation of patient, recent occupation of patient, and presence in the home of people currently suffering from physical or psychiatric disorder. In the total sample of 236 patients adjusted for treatment difference, no relationship with relapse/readmission was found for any of these variables. When the trial sample alone was considered, in placebo patients, a higher degree of social withdrawal was associated with relapse ($X^2=6.21$, df$=2$, $P=0.045$) and in all trial patients adjusted for treatment, relapse was associated with onset >1 month as compared with <1 month and <7 days ($X^2=12.5$, df$=2$, $P=0.002$). In all trial patients adjusted for treatment, relapse was associated with the presence in the home of physically or psychiatrically ill people ($X^2=7.17$, df$=2$, $P=0.028$).

Employment

At the conclusion of the study, 62 patients were in full-time employment, 22 were full-time housewives, five full-time students, 87 unemployed, 11 in irregular employment (i.e. undeclared or illegal work), and no information was available in 34 cases. The remainder were dead or in judicial custody.

Marriage and child care

Of those alive at follow-up, 168 were single, 45 married, 13 divorced, 11 separated, seven cohabiting and five widowed. Five patients (two males, three females) married during the course of the study and three males entered into

TABLE II
Status of patients at conclusion of study[+]

Patient groups	*Entered in study*	*Relapse-free/readmission*		*Relapsed readmitted*	*Actuarial % relapse-free/readmitted (standard error*[*]*) at (months)*			
		complete follow-up	*incomplete follow-up*		*6*	*12*	*18*	*24*
Period between onset and discharge <1 year								
Eligible	58	10	27	21	63 (7)	60 (7)	48	48
Active	31	18	3	10	80 (7)	80 (7)	71 (9)	57
Placebo	49	18	6	25	70 (7)	46 (8)	43 (8)	43
Sub total	138	46	36	56	70 (4)	60 (5)	52 (5)	48 (5)
Period between onset and discharge >1 year								
Eligible	33	4	23	6	87 (6)	77 (9)	77	77
Active	22	5	2	15	76 (9)	33	26	18
Placebo	15	0	1	14	30	8	—	—
Sub-total	70	9	26	35	71 (6)	44 (7)	38	30
Period not known								
Eligible	25	2	17	6	70 (11)	70	70	—
Active	1	0	1	0	—	—	—	—
Placebo	2	0	0	2	—	—	—	—
Sub-total	28	2	18	8	69 (11)	69 (11)	69	—
All patients								
Eligible	116	16	67	33	72 (5)	67 (5)	60 (6)	54
Active	54	23	6	25	79 (6)	61 (7)	53 (8)	42
Placebo	66	18	7	41	60 (6)	37 (6)	33 (6)	30
Total	236	57	80	99	70 (3)	56 (4)	49 (4)	42 (5)

[+] Either 2 years from discharge or 01.08.82, whichever earlier

[*] Standard errors given when number of patients at risk exceeds ten

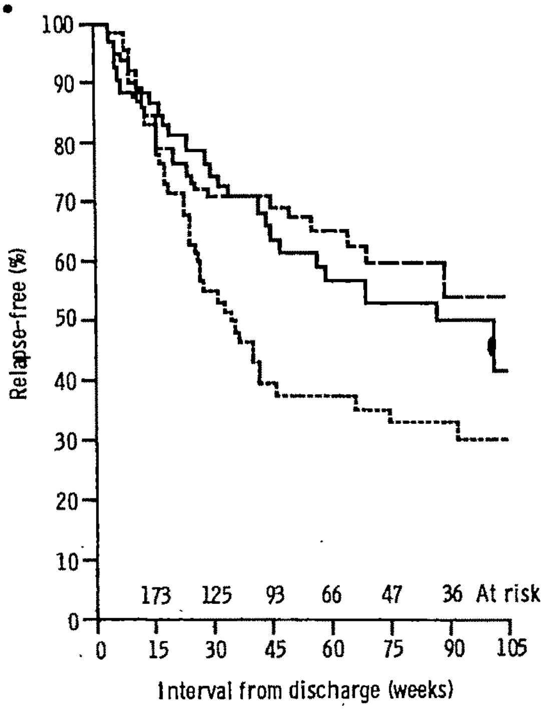

FIG. 1 Actuarial percentage relapse-free curves for trial patients on active (——, 54 patients) and placebo treatment (——, 66 patients) and for trial eligible patients (————, 116 patients)

stable cohabiting relationships. Two male patients did not enter into marriage already arranged for them, the arranged marriage of a male patient ended in formal divorce, and another male patient became legally separated. One further marriage ended when a male patient murdered his wife while in a psychotic state.

Of the 253 patients, 63 were known to have had children at admission, and three gave birth during follow-up. The 66 parents had a total of 119 children, of whom 85 were minors, these being the children of 53 patients.

At admission, 23 of the 35 children of male patients lived in the nuclear family, one lived with the father only and 11 with the mother only. At follow-up, 17 lived in the nuclear family, 15 with the mother alone and 3 were in care. Of the 47 children of female patients at admission 24 lived in the nuclear and 3 in the extended family 14 with the mother alone, one with the father alone and 5 were in care. Of the 50 children at follow-up 24 lived in the nuclear and 6 in the extended family and 11 with the mother alone. Seven were in care and 2 lived abroad in unknown circumstances.

Judicial contact

Among the 17 non-discharged patients, one was transferred to Broadmoor Maximum Security Hospital, and three remained under Section 60 of the Mental Health Act.

Judicial charges of murder, actual bodily harm, malicious damage, indecent exposure, theft, and illegal immigration were brought in the case of seven discharged patients, and a Section 60 was requested for one other patient.

Discussion

Outcome can be considered in terms of employment social function, severity of symptomatology, and duration of hospitalisation after initial diagnostic evaluation (Strauss & Carpenter, 1974; Stephens, 1978). About 50% of the patients in the present study were employed at follow-up, compared with 65% in the study of Cooper (1961) and 59% in that of Nyman & Jonsson (1983). These figures probably reflect differences in employment possibilities in England in the 1960s and the 1980s and between England and Scandinavia. Social function is difficult to assess (Weissman, 1981) and in this study was not formally rated; the assessments are confined to information relating marriage, child care, and judicial contact. Only 50% of the children who were minors lived in a nuclear family setting: there is no control group from the population from which the study sample was drawn, and it is not possible to determine to what extent this reflects the breakdown of traditional patterns of society; but in part, it must represent the social cost of schizophrenic illness. The association between schizophrenia and violent and other crime is well known (Taylor & Gunn, 1984; Weller, 1984); judicial contact in the present sample may represent no more than might be expected from past work. The fact that a patient not previously considered dangerous murdered his wife, despite close supervision and active medication, should not be overlooked.

Severity of symptomatology is assessed in terms of relapse in the trial patients and of readmission in the trial eligible patients; it could be argued that relapse and readmission are not necessarily related to severity, but in the trial sample, relapse was associated with the development of psychotic features in the great majority of cases (Crow *et al*, 1985). Relapse occurred in about 60% of patients. It is difficult to compare relapse rates in the trial and trial-eligible patients because contact with so many of the latter was lost: in patients with a duration between onset and discharge of more than one year, contact in trial-eligible cases was maintained in less than one third. The suicide rate in schizophrenia is substantially in excess of that in the general population (Markowe *et al*, 1967). Using results from a recent study in which three out of 39 first-episode schizophrenic patients were found to have killed themselves over a 10–15 year follow-up period, Wilkinson (1982) calculated an estimated annual rate of suicide in a first-admission sample of schizophrenics of between 500 and 750 per 100,000 (i.e. 1/130–200). If it is assumed that four of the 253 patients who died during the two-year follow-up period killed themselves, the suicide rate is in keeping with the above figure. The duration of inpatient care was counted to the point of discharge; 17 patients did not achieve discharge at all, and a further 34 required inpatient care for over six months. These 51 patients came from all of the hospitals participating in the study and the prolonged admissions were not, therefore, treatment policy, but resulted from unremitting illness.

Thus, even at this early stage of schizophrenia, the outcome for many patients is poor, but nonetheless, it was not poor in every case. The median age of this sample is 25 years, a time of life at which educational, occupational, and social achievement might be expected; from the information available at follow-up, it was possible to make some assessment of this. Ten cases made definite attainments: two completed further education courses (one obtained a degree at art school and one completed his apprenticeship as a toolmaker), one completed 'O' levels at night school, three achieved promotion at work (a musician, a lecturer, and in the motor manufacturing industry), two entered stable cohabitation, and one achieved work compatible with his high premorbid intelligence and resumed his PhD. Three additional cases achieved less; one limited youth started an industrial rehabilitation course, one man who had never previously lived alone maintained his former occupation as a dustman and lived in his own flat, while a third man (previously a university undergraduate) obtained a place at polytechnic. Thirteen patients thus made definite or possible achievements, but in the remainder, there is no record of activity which could be classed as achievement even in these modest terms. Eleven of the thirteen patients were trial entrants (nine on placebo and two on active medication), while two were trial-eligible and received standard medication. Although this part of the study was not controlled, the excess of achievers on placebo as compared with active medication is compatible with the possibility that the price of the reduced risk of relapse conferred by neuroleptics is a decline in achievement. This possibility deserves thorough investigation in an appropriately controlled study.

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IV. Expressed Emotion and Relapse

J. F. MacMILLAN, A. GOLD, T. J. CROW, A. L. JOHNSON AND E. C. JOHNSTONE

The relatives of 82 patients in a study of first episodes of schizophrenia were interviewed within six weeks of the index admission; 77 patients were subsequently discharged, and were followed to relapse or readmission. Analysis of relapse-free survival time was used to examine whether the components of 'expressed emotion' predicted relapse or response to neuroleptic medication: 'critical comments' by relatives was the only component present often enough to be used and was inversely related to 'social contact'. When pre-admission duration of illness, and neuroleptic medication following discharge (identified previously as significant predictors of outcome) were taken into account, neither 'critical comments' nor 'social contact' were related to outcome nor to response to medication. The constellation of factors suggested as pathogenic was present only in a minority of cases: many patients lived alone and of those that were with families, most were not in high face-to-face contact with other members. The failure of the components of 'expressed emotion' to predict outcome or response to neuroleptic medication suggests that at best, such factors are weak predictors of liability to relapse. Their influence is unlikely to be comparable in magnitude to that of neuroleptic medication.

Whereas theories of the psychogenesis of schizophrenia have received little experimental support, there is a substantial body of research on the role of psychological factors in precipitating relapse. Much of this relates to the concept of 'expressed emotion' (EE), developed as an index of the emotional impact of relatives on the patient (Brown & Birley, 1968). Brown *et al* (1962), found EE in the relatives better correlated than EE in the patient with the probability of relapse, and Brown *et al* (1972) also found that high EE predicted relapse, particularly in those patients in close contact with their relatives. Vaughn & Leff (1976) developed the concept that high EE in, and close contact with relatives was causally related to relapse, and that neuroleptic medication played a role in preventing this sequence (Leff & Vaughn, 1981). Leff *et al* (1982), in a small clinical trial, attempted to reduce EE in relatives in high contact by a strategy of social intervention; they reported success in reducing critical comments (CC), over-involvement, or social contact (SC) in the relatives of some patients and that in these patients, relapse rates were reduced. On this basis, it is argued that a causal role in precipitating relapse has been established for EE in the relatives, and thus that a major determinant of outcome in schizophrenia has been identified. Such a conclusion would have potential implications for understanding the schizophrenic disease process.

A number of considerations though, make the findings of this study less decisive than they might otherwise be: the number of patients was extremely small—13 in each of the treatments groups, not all of whom completed the study, and in only three cases was relapse of sufficient severity to require admission. It was not feasible to keep assessment of relapse blind to the social intervention status of patient and family, and an independent assessor did not always concur with the view of the clinician that a relapse had occurred. These facts make it doubtful whether the postulated causal connection between expressed emotion and relapse can be regarded as fully established. A problem with the studies of EE is that they have been carried out on groups of patients at various stages of the disease, including those who have experienced previous episodes, as well as a smaller proportion following first episodes; that high EE leads to relapse is not the only possible explanation of a relationship between these variables, for instance severity of illness might lead to heightened EE in close relatives. Our study of a large series of patients suffering from a first episode of schizophrenic illness (Johnstone *et al*, 1985; Crow *et al*, 1985) provided an opportunity to examine the relationship between EE in the relative and SC between relative and patient on the one hand, and relapse at an early stage of the disease on the other. Thus, the hypothesis that high EE/SC causes schizophrenic relapse could be examined in a situation where expectation of the outcome of the illness and the relatives' attitude to it was not contaminated by experience of repeated relapse. Because the study included a placebo-controlled drug trial, it was also possible to examine the relationships between EE/SC, relapse, and neuroleptic administration, and to relate outcome to additional variables.

Method

The Camberwell family interview

The Camberwell Family Interview (CFI) was developed in the MRC Social Psychiatry Unit (Brown & Rutter, 1966; Vaughn & Leff, 1976). 'Expressed Emotion' is assessed in terms of four main components: critical comments, over-involvement, hostility, and warmth, of which the first two are regarded as the crucial measures (Leff & Vaughn, 1980). In this study, the CFI was conducted by a research worker (A. G.), trained by Ms E. Kuipers of the Social Psychiatry Unit, who herself blindly rated 12 of the tapes. There was no disagreement between the two in the rating of EE, using a cut-off of six (four high; eight low) and disagreement in only one case in the rating of SC, using a cut-off of 35 hours (AG four high; eight low; EK five high; seven low). A time budget of hours per week of face-to-face contact between relative and patient established levels of SC as has been done previously.

The interview was conducted within six weeks of the patient's admission. The research psychiatrists and collaborating clinicians remained blind to these assessments, and the interviewer remained blind to any assessments of the patients.

The Disturbed Behaviour Rating (DBR) Scale

Each of the five items (Johnstone *et al.* 1985) was rated on a four-point scale, as absent (0), occurring once (1), or more than once (2) over the period of one month before admission, or present repeatedly or for more than one month before admission (3). This rating thus included both a severity and a duration assessment. To avoid contamination with the factor of duration of symptoms before admission (which was found to be an important determinant of relapse), a revised form of rating was devised in which the temporal element was removed and each of the five items was rated as absent (0) or present (1), giving a total DBR range from 0 to 5.

Sample of patients and their relatives

The patients were drawn from those included in the multi-centre study of prophylactic neuroleptic medication, following first episodes of schizophrenia.

TABLE I

Derivation of samples for assessment of disturbed behaviour and Expressed Emotion

First schizophrenic episodes	*Trial entrants 120*	*Trial-eligible 133*		*Total 253*	
Not assessed					
Living alone	—	19		19	
Unassimilated immigrant background	—	3		3	
Patient/relative refusal	—	4		4	
Other reasons*	—	4		4	
Sub-total	—	30	(3)	30	(3)
*Expressed Emotion only assessed****	—	1		1	
DBR assessed	120	102	(10)	222	(10)
Subgroup not assessed for Expression Emotion					
Living alone	33	29		62	
Unassimilated immigrant background	20	13		33	
Patient/relative refusal	10	21		31	
Other reasons**	6	9		15	
Sub-total	69	72	(5)	141	(5)
Assessed on both	51	30	(5)	81	(5)

Figures in brackets are numbers of patients not discharged from hospital by 30.4.82.

*Details of "other reasons"—1 relative on staff of hospital: 2 patients went to private or other care elsewhere; 1 landlord died.

**Details of "other reasons"—6 trial cases—2 relatives ill: 2 relatives on holiday: 1 very early discharge: 1 case matrimonial disharmony so severe that interview was not sought; 9 trial eligible cases—1 relative on holiday; 6 very early discharge; 2 technical reasons.

***DBR not assessed because 1 patient (paranoid jealousy) refused to have his wife see a psychiatrist but permitted A. G. to visit.

The CFI is applicable only when the patient has lived with others for three months or longer, immediately preceding admission, and where the relatives' English is such that communication adequate for an extended interview can be established. Thus, patients who lived alone and those from unassimilated immigrant backgrounds could not be included, although first- and second-generation immigrants and patients of all racial origins were considered as potential candidates. The derivation of the sample assessed with the DBR and CFI, and its relationship to the samples of trial entrants and trial-eligible patients are presented in Table I.

Demographic characteristics including age, sex, marital status, and employment, the racial origin of the patient, and main informant, and the relationship of informant to the patient are summarised in Table II.

TABLE II

Characteristics of Patients and Relatives

	DBR assessed		*EE assessed*	
Total	222	(10)	82	(5)
Sex				
Male	129	(5)	48	(2)
Female	93	(5)	34	(3)
Racial origin				
White European	151	(10)	68	(5)
West Indian Negro	36		6	
African Negro	6		2	
Asian	22		2	
Oriental	1		—	
Mixed	6		4	
Mother tongue				
English	185	(9)	78	(4)
European	11	(1)	2	(1)
Oriental	1		—	
Indian	19		1	
Other	6		1	

Statistics

Two distinct analyses were undertaken, one to investigate inter-relationships between the disturbed behaviour and assessments of EE, and the other to relate these scales to

TABLE II (*continued*)

	DBR assessed		*EE assessed*	
Hospital				
Northwick Park	49	(3)	24	(3)
Luton and Dunstable	47	(1)	23	
Shenley and Wembley	68	(3)	15	(2)
Hill End	13		7	
St. Bernard's and St. John's	11	(1)	3	
St. Mary's	13		3	
Napsbury	3		3	
Friern. Royal Free Whittington & Chase Farm	18	(2)	4	
Age at admission (years)				
15–19	32	(2)	19	(1)
20–29	115	(4)	41	(1)
30–39	44	(3)	18	(3)
40–49	20	(1)	4	
50–59	10		—	
60–65	1		—	
Median (range)	24.4	(15–65)	23.3	(16–46)
Period of onset (months)				
<1	47.1	(1)	14	
1–2	21	(1)	7	(1)
2–6	58	(1)	24	
6–12	18		8	
12–24	24	(2)	14	(2)
24–48	12	(3)	7	(1)
48–	17	(2)	7	(1)
Not known	16		1	
Median (range)	4.1	(1 week –16 years)	4.8	(1 week –16 years)
Period of hospital admission (weeks)				
<2	7		—	
2–3	11		3	
3–4	12		3	
4–8	59		21	
8–12	38		15	
12–	85		35	
Not discharged	10	(10)	5	(5)
Median (range)	8.9	(1.5–80)	9.4	(2–80)
PSE				
S+	178	(5)	64	(2)
P+	28	(4)	9	(2)
P?	6		2	
O+	1		—	
D+	6		4	
Not known	1		1	
Employment at admission				
Employed, full time	96	(1)	24	
Employed, part time	2	(2)	1	
Housework, full time	28	(2)	2	
At school	15		9	
Unemployed	18	(5)	46	
Marital status at admission				
Single	162	(7)	59	
Married	40	(2)	16	
Divorced, separated or widowed	12		6	
Cohabiting	8	(1)	1	
Informants				
Living with patient for 3/12 or more	134	(7)	82	(5)
Living with patient for <3/12	7			
Not living with patient	27	(2)		
No informant/patient only	54	(1)		
Informant				
Both parents	24	(3)	6	
Mother	69	(2)	46	
Father	16	(1)	8	
Husband	25	(2)	12	
Wife/cohabitee	10		5	
Brother	4		1	
Sister	8		3	
Sister-in-law	1		1	
Other	11	(1)		
None (patient only)	54	(1)		
Racial origin of informant				
English	115	(8)	63	
Italian	2		2	
Polish	6		4	
Swiss	1		1	
Greek	3	(1)	1	
Asian	18		2	
Negro	21		9	
Mixed/Other	2			
Disturbed behaviour rating				
0	40	(1)	12	
1	79	(3)	27	(1)
2	54	(4)	19	(2)
3	36	(1)	15	(1)
4	12		7	
5		(1)	1	(1)
Not rated	—		1	
Expressed emotion critical comments				
0–2			18	
3–5			18	
6–8			17	(2)
9–11			14	(2)
12–14			6	
15–17			7	(1)
18–			2	
Median (range)			6.9	(0–20)
Social contact				
>35 hours			22	(1)
<35 hours			60	(4)

(Figures in brackets, except for ranges, are numbers of patients not discharged from hospital.)

relapse/readmission. In both analyses, the assessments of EE were dichotomised, using cut-off points of six for critical comments and 35 hours for social contact (Vaughn & Leff, 1976). Ratings of disturbed behaviour were categorised as described below.

Relationships between the three assessments were investigated by fitting log-linear models to the cell frequencies (incremented by 0.5 to avoid zeros) of three-dimensional contingency tables (Everitt, 1977). Two analyses were performed: one with DBR dichotomised, using a cut-off point at 1 (giving a $(2\times 2\times 2)$—contingency table constructed from DBR ($\leqslant 1$, $\geqslant 2$), critical comments (<6, $\geqslant 6$) and SC (<35 h, >35 h); the other with DBR categorised in three groups as 0, 1 and 2, and 3 or more (giving a $(3\times 2\times 2)$—contingency table). In both analyses, the model containing all main effects and interactions (saturated) was fitted to the cell frequencies, and subsequently reduced hierarchically by eliminating the three-factor interaction, two-factor interactions, and main effects (using the computer package GLIM (Baker & Nelder, 1978), where the exclusion of the factors resulted in a non-significant ($P>0.05$) increase in the maximum likelihood chi-squared statistic.

To investigate associations with relapse/readmission, the period from hospital discharge to relapse/readmission, loss to follow-up, or 1 August 1982 (up to a maximum of two years) was calculated for each patient: the resultant relapse-time distributions were summarised using actuarial "life-table" techniques. Comparisons between sub-groups or patients were made using the logrank test (Peto *et al*, 1977). Separate actuarial analyses were performed for disturbed behaviour (four sub-groups: 0, 1, 2 and at least 3), CC, and SC. Since both treatment (active/placebo) and period between onset of illness and admission to hospital (<1 year, >1 year) are of prognostic importance (Crow *et al*, 1985), the comparison of the separate groups has also been performed controlling for these variables. To quantify non-significant ($P>0.05$) differences, the Cox proportional hazards model (Cox, 1972) incorporating period between onset of illness and admission, and the appropriate rating variable as covariates has been fitted to the data, and an estimate (with 95% confidence interval) obtained of the hazard rate ratio.

Findings

1. *The Camberwell Interview: Critical comments, over-involvement, and social contact*

The median number of critical comments expressed by the relatives in the course of a two-hour or more interview was 6.9, and ranged from zero (five relatives) up to 20 (Table II), in a positively skewed distribution. Fifty of the 88 relatives (single relative for 76 patients and both parents for six patients (Table III) assessed exceeded the criterion of six or more critical comments, defined by Vaughn & Leff (1976) as the cut-off between those of "high" as compared to "low" EE.

The number of "over-involved" comments made by this population of relatives was small—76 out of the 88 relatives making no such comments. Of the 12 who did make such comments, only three relatives exceeded the criterion of three suggested by Leff *et al* (1982) as the entry qualification for high EE ranking on grounds of over-involvement alone; all three had already qualified by their CC performances; and two of these (both mothers) were probably themselves psychotic.

SC was assessed in terms of face-to-face contact between relative and patient in a typical week before admission: 22 patients were in high (greater than 35 hours) social contact; and this was unrelated to the number of people in the household or the social class of father or spouse.

2. *Relationship between Camberwell Interview and disturbed behaviour rating*

Disturbed behaviour ratings were available on 81 of the 82 patients whose relatives were assessed for EE, with possible scores ranging from zero to 15 (representing a maximum score of three on each of the five items). The revised DBR rating eliminating duration reduced the range to five, and the relationships between DBR, CC and extent of SC were assessed from the data displayed in Table III.

TABLE III
Distribution of patients by disturbed behaviour rating (DBR) and critical comments and social contact

		Social contact		
		<35 h	*>35 h*	*Total*
DBR=0				
Critical	<6	4	3	7
Comments	≥6	5	0	5
DBR=1				
Critical	<6	6	6	12
Comments	≥6	14	1	15
DBR=2				
Critical	<6	6	4	10
Comments	≥6	8	1	9
DBR=3, 4 or 5				
Critical	<6	4	2	6
Comments	≥6	12	5	17
Sub-total				
Critical	<6	20	15	35
Comments	≥6	39	7	46
Total		59	22	81

The two methods of analysis (one with DBR dichotomised and the other with DBR sub-divided into three groups 0, 1 and 2, and 3 or more) gave consistent results. In both models, the three-factor interaction and the two-factor interactions involving disturbed behaviour could be eliminated. In the first analysis (DBR dichotomised) the main effect of this variable could also be eliminated, leaving a model incorporating the two EE ratings and their interaction ($X^2=3.96$, df=4, $P>0.40$). In the other analysis, the main effect of DBR could not be eliminated ($X^2=20.6$, df=2, $P<0.001$), reflecting the uneven distribution of patients across the three levels of DBR. The data are consistent with a model of partial independence ($X^2=7.56$, df=6, $P>0.20$), with DBR unassociated with either CC or SC. In either analysis, it is permissible to collapse the tables over the levels of DBR without introducing false associations. The resultant 2 × 2 table indicates that a higher level of CC from the relatives was associated with a lower level of SC with the patient. ($X^2=7.72$, df=1, $P<0.01$).

3. *Expressed emotion, social contact and disturbed behaviour as predictors of relapse and readmission*

Of the 82 patients who had been assessed in the home environment with the CFI, 77 achieved discharge. Those who entered the prophylactic drug trial were followed to relapse, loss of contact, the lapse of two years, or the close of the study. The 26 patients who did not enter the trial and received standard outpatient care were reviewed at the close of the larger study; in these cases, readmission served as the closest parallel to relapse, as defined in the protocol. The numbers within each of these groups, sub-divided by the components of EE, are tabulated by outcome in Table IV.

Comparison of relapse rates in the two CC groups revealed higher relapse/readmission rates in the group with a score of six or more (logrank test: $X^2=4.40$, df=1, $P=0.036$), but this difference is related to the prognostic factors of duration of illness preceding admission and neuroleptic treatment following discharge (adjusted

TABLE IV

Outcome related to expressed emotion (critical comments) and social contact assessed in the Camberwell Interview for patients discharged from hospital

Critical Comments	*Treatment*	*No. of patients*	*Relapsed*	*Relapse free Lost to follow-up*	*Complete follow-up*
<6	Active	14	7	0	7
	Placebo	10	6	0	4
	Standard	12	1	2	9
	Sub-total	36	14	2	20
≥6	Active	9	6	2	1
	Placebo	18	14	0	4
	Standard	14	6	1	7
	Sub-total	41	26	3	12
	TOTAL	77	40	5	32
Social Contact					
<35	Active	18	13	1	4
	Placebo	22	16	0	6
	Standard	16	4	2	10
	Sub-total	56	33	3	20
>35	Active	5	0	1	4
	Placebo	6	4	0	2
	Standard	10	3	1	6
	Sub-total	21	7	2	12
	TOTAL	77	40	5	32

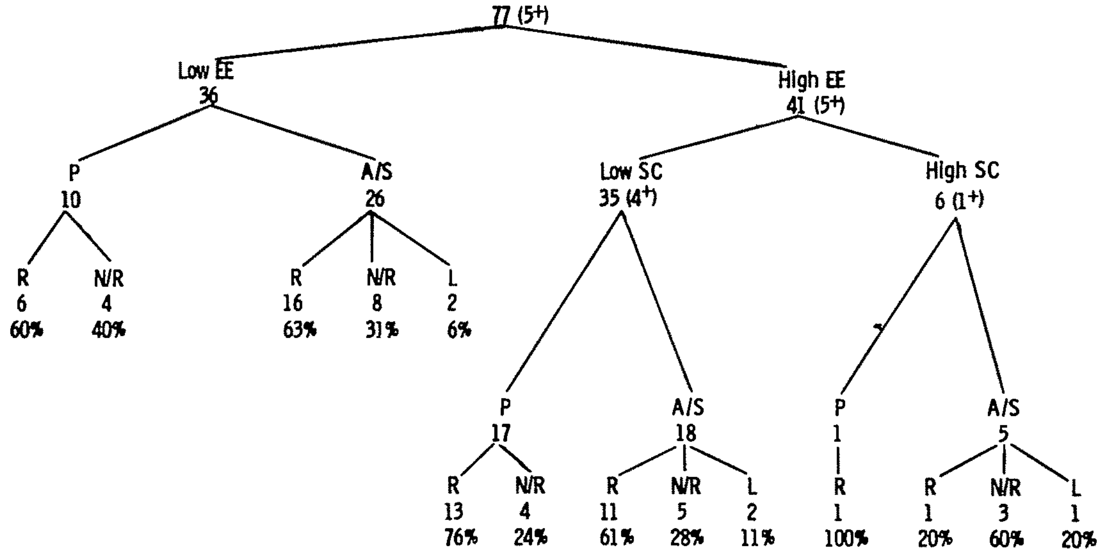

FIG. 1 Branching diagram of relapse rates in patients divided by expressed emotion and allocation of medication.

EE = Expressed Emotion; SC = Social Contact; P = Placebo medication; A/S = Active or standard medication; R = Relapsed; N/R = Not relapsed at conclusion of study; L = Lost to contact. Numbers represent individual cases; those in brackets refer to patients not discharged from hospital.

$X^2 = 2.21$, df = 1, $P = 0.14$). The patients in the high CC group included more who were allocated to placebo and more with a long duration of illness before admission. The 36 patients with critical comments of less than 6 consisted of 29 patients with an interval between onset and admission of less than 1 year, 6 in whom this interval was more than 1 year, and one in whom the duration of this interval was unknown. Of those with the shorter interval 20 were on active or standard treatment and 9 on placebo; of those with the longer interval 5 were on active or standard treatment and one on placebo. The 41 patients with critical comments of six or more consisted of 23 patients with an interval between onset and admission of less than 1 year and 18 patients in whom it was more than 1 year. Of those with a shorter interval 10 were on active or standard and 13 on placebo treatment, of those with the longer interval 13 were on active or standard and 5 on placebo treatment. There was no significant association between number of critical comments and the allocation of the medication but there was a significant relationship between the number of critical comments and the duration of the onset to admission interval such that higher critical comments are associated with the longer interval ($P = 0.012$). It is likely that these two variables are not independent. There was no significant difference between relapse rates in the two social contact groups ($X^2 = 1.69$ df = 1 $P = 0.19$; adjusted for treatment and duration of illness $X^2 = 1.93$, df = 1, $P = 0.17$).

The hazard rate ratio, calculated using the Cox proportional hazards model (Cox 1972), incorporating treatment and the period between onset and admission was 1.7% (95% confidence limits: 0.8.3.4) for low compared with high SC, and 1.8 (0.7, 4.2) for high compared with low CC. Thus, the hazard rate in the low SC group is 1.7 times that in the high SC group (but could be anywhere between 0.8 and 3.4); the width of the 95% confidence limits indicates the difficulties of interpreting these non-significant relationships.

Comparison of the relapse/readmission rates in the four DBR groups indicated no important differences between them ($X^2 = 2.35$, df = 3, $P = 0.50$), even after adjustment for treatment and pre-admission illness duration ($X^2 = 1.80$, df = 3, $P = 0.62$).

Discussion

Neither of the two components of the CFI emerged from this study as important determinants of relapse/readmission significant at the 5% level: while duration of illness prior to admission and neuroleptic medication after discharge are related to relapse (Crow *et al*, 1985), the level of CC made by the relatives and the SC between relatives and patients may not be. There is a significant association between longer duration of illness prior to admission and higher CC, the causal sequence of which is unclear.

In two respects, this study provides a more critical test of the role of social factors in determining outcome than the earlier investigations. Firstly, patients have been examined at an earlier stage, when the role of aetiological factors might be expected to be more evident, and the population is more homogeneous. Secondly, the assessments of the CFI and of the patients themselves with respect to clinical variables and relapse have been conducted by independent workers and blindly.

Some findings with the CFI may reflect the stage of the disease: as previously recorded, (Leff *et al*, 1982) over-involvement was unusual and added nothing to CC in contributing to EE; SC with relatives however, was relatively low, exceeding the 35 hours used in previous studies as a cut-off for high face-to-face contact in only 21 out of 77 cases. Brown *et al* (1972), found this figure exceeded in 52 of their 93 cases, and Vaughn & Leff (1976) in 23 of their 37 cases, so that high SC may be a factor which increases with chronicity of the disease. In this study, SC was inversely related to the level of CC expressed by the relatives; one may suspect that where the behaviour is intolerable to the relative, SC between patient and relative will be low.

The findings of this study offer little support to the view (Vaughn & Leff, 1976) that EE in relatives can be used to predict response to neuroleptic medication. Analyses of the numbers of patients who relapse in relation to neuroleptics and the CFI factors as a branching diagram (as such findings have previously been presented. Vaughn & Leff, 1976) reveals some of the difficulties of this concept (Figure 1). Firstly, the sample of patients in whom EE can be assessed is reduced because a number (81) are living alone, while a further proportion (36 patients) are of unassimilated immigrant background and, because of language problems, cannot be assessed in this interview. In a number of further cases, cooperation was refused and a further proportion (five cases) did not achieve discharge from hospital. Thus, the 77 patients in whom EE can be assessed represent only 30.4% of the original sample of patients who were eligible on account of a PSE diagnosis of schizophrenia. Of this population of 77 patients, 41 relatives are classified by the CC cut-off rating of six as manifesting high, and 36 as showing low EE. However, further sub-division of these groups by high and low SC reduces the numbers in each cell (particularly those in high contact with relatives) to such small magnitudes that assessment of the effects of medication within these sub-groups is rendered hazardous (Figure 1).

A crude examination of the percentage relapse/readmission rates in the present study reveals results apparently discrepant with earlier work (Vaughn & Leff, 1976). Such simple comparisons take no account of duration of time that each patient is free from relapse/readmission (which is accommodated by the survival analysis in the present study) or the variable of duration of illness before admission, (which is here taken into account in calculating the adjusted X^2 values relating to SC and CC as predictors of relapse/readmission.)

There are difficulties for the view that predictors of response to medication can be identified in the family environment. Leff & Vaughn (1981) reported that whereas in their earlier sample high EE predicted relapse in the nine months following discharge, and identified a group for whom neuroleptic medication was particularly indicated, when follow-up of those who were well at nine months was extended to two years, EE no longer predicted relapse. Moreover, significant effects of neuroleptic medication were now apparent in the survivor group that were of greater magnitude in the low- than in the high-EE sub-samples. Thus, survival following discharge is a relevant variable, and this can be most accurately assessed by the actuarial analysis of relapse-free time, as in the present study.

EE has only previously been considered in the various studies associated with the MRC Social Psychiatry Unit, but other controlled studies (Hogarty *et al*, 1973, 1974, 1979; Goldstein *et al*, 1978; Falloon *et al*, 1982) have examined the possibility that family intervention may reduce relapse rates following schizophrenic episodes. The nature of the intervention varies between studies, but all include some form of social support or counselling for the relatives, and share common ground with methods used by Leff *et al* (1982), to reduce EE. Although Hogarty *et al* and Goldstein *et al* report positively, the study of Falloon *et al* perhaps provides the most impressive evidence of a beneficial effect from family intervention (Barrowclough & Tarrier, 1984). Although the effect in Falloon *et al's* study may be due to a reduction in EE, the authors themselves draw attention to other interpretations, which include demonstrated increased compliance with medication in the family treatment group (Strang *et al*, 1981) and the possibility of greater tolerance of deviant behaviour resulting from support provided for the family. We do not wish to suggest that support and counselling are not worthwhile, and indeed consider them a necessary feature of the management of schizophrenic patients, but their role in determining outcome has yet to be demonstrated.

Although the findings of the present study are not decisive (we have drawn attention to the uncertainties surrounding the estimates of hazard rate ratio), we regard them as casting considerable doubt on recent speculations that important predictors of outcome are present in the family environment. If such factors exist, it is not clear why they should not have been more apparent in the present relatively homogeneous and well documented population of patients with early schizophrenia, although of course they might emerge from more extensive studies. On the other hand, some correlations between family factors and relapse rates, reported in the recent literature, may arise not from a direct causal relationship between critical comments made by the relatives and re-emergence of positive symptoms, but from more complex relationships between the severity of the disease, the burden placed on the immediate relatives, and their response to it. Such an interpretation would be undermined by an unequivocal demonstration that by modifying the family environment, the outcome of the disease is significantly altered. The most important clinical implication of the findings present, however, is to introduce a note of caution toward enthusiastic and generalised therapeutic interpretations of studies of the family environment in schizophrenia. If genuine determinants of poor outcome are present in the immediate families of patients with schizophrenia, they are somewhat elusive and when present, their effects are unlikely to be large. The search for such influences should not detract from the much better documented, although limited prophylactic effects of neuroleptic medication.

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*Eve C. Johnstone MD FRCP, FRCPsych, *Member of Scientific Staff and Honorary Consultant Psychiatrist, Northwick Park Hospital and Clinical Research Centre, Watford Road, Harrow, Middlesex HA1 3UJ.*

Timothy J. Crow PhD, FRCP, FRCPsych. *Head of Division and Honorary Consultant Psychiatrist, Northwick Park Hospital and Clinical Research Centre.*

Anthony L. Johnson BSc, PhD, FIS *Medical Statistician, MRC Biostatistics Unit MRC Centre, Hills Road, Cambridge CB2 2QH.*

J. Fiona Macmillan MB ChB, MRCPsych *Formerly Member of Scientific Staff and Honorary Senior Registrar, Northwick Park Hospital and Clinical Research Centre, Now Senior Lecturer, Department of Psychiatry, University of Birmingham.*

Aviva Gold, SRN, SCM, Dip Soc. Sci, *Formerly Senior Social Worker, Division of Psychiatry, Northwick Park Hospital and Clinical Research Centre.*

*Correspondence

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The 'Italian Experience' Reconsidered

KATHLEEN JONES and ALISON POLETTI

Our analysis of the problems of the Italian psychiatric services has drawn a lively correspondence challenging our findings. In September 1985, we undertook a second study tour in Italy. This is now reported, with notes on specific criticisms of the earlier paper.

The story of the 'Italian Experience' in attempting to abolish mental hospitals and replace them with 'alternative structures' in the community has drawn international attention, because no other country has adopted such an extreme policy by statute. In Britain the policy has been highly praised by a number of observers (Hanvey, 1978; Ramon, 1982; Daniels, 1983; Lacey, 1984; Heptinstall, 1984) who have seen it as a paradigm for British policy.

The query raised in our minds after studying the Italian literature on the subject related not to the experimental services in Trieste, where the reforms began, but to whether the movement was sufficiently widespread and sufficiently successful to be described as a national policy. It seemed clear that the law of 1978 (No. 180, now part of Law No. 833) was being hotly debated, and that there were many places in which it was not working well. Statistics were of little guidance, since they were dated and lacked explanatory power. Empirical testing seemed the only feasible approach, and we travelled 800 miles through Italy, visiting Como, Milan, Pavia, Pisa, Lucca, Florence, Salerno and Reggio di Calabria in a line from the north to the south of the country. We knew that there were supporters of the new law in Milan, and opponents in Pisa. For the rest, our choice of centres was dictated wholly by geography.

In each city, we worked through the *primario*, or consultant in charge of a service. We investigated Diagnosis and Cure (D & C) units in general hospitals, community services, university clinics and mental hospitals. We did not visit Trieste, which had been well-publicised, or Rome, which was too large to comprehend in the limited time available.

Our conclusions were that Trieste was not Italy. The new law had created many difficulties in a country where most of the psychiatric services were chronically starved of resources, and only the Communist Party continued to support it. The other major parties had drawn up proposals for legal revision, which involved the use of the old mental hospitals for medium or long-stay care.

Publications (Jones & Poletti, 1984; Jones & Poletti, 1985a, b) drew considerable professional interest. In the last of these papers in the *Journal* we did not repeat the descriptive material of earlier ones, but attempted to consider the question why, when the real facts about the Italian situation were readily accessible, British observers continued to repeat the myth of unqualified success.

Criticisms

Our *Journal* paper has drawn a somewhat vehement correspondence from the supporters of Psichiatria Democratica. It has been stated, *inter alia*, that we are "in favour of mental hospitals" (Tansella, 1985); that we gave "an inaccurate picture of Trieste" (Ramon, 1985), and that we predicted "the certainty of catastrophe for any country if mental hospitals are abolished" (De Girolamo, 1985). Perhaps these comments will give readers some idea of the general flavour of debate. Neither of us is in favour of mental hospitals, provided that better forms of care can be devised for patients; what matters is the quality of care, not where they are housed. We gave no description of Trieste at all, because we had not visited Trieste; and the comment about "predicting catastrophe" can only be a linguistic misunderstanding. What we did was to set down a series of hypotheses which required testing, and to say that the evidence was insufficient to test them. The main complaint was that we had not been to Trieste, and that instead of taking a longitudinal section through Italy (which gave us some idea of how the law was working), we should have followed the practice of other observers and seen the new system at its best.

We thought that this misinterpreted our intentions. We had been concerned about the descriptions of the reforms as 'the Italian Experience', when it was comparatively easy to show that they did not apply in much of Italy. It was therefore a question of social policy, of studying the implementation of a law; we had not commented at all on 'The Trieste Experience', merely pointing out that Trieste was not Italy. However, we were prepared to learn; and in September 1985, we spent a further three weeks in Italy, visiting services in Trieste, Rome, Ferrara, and Bologna—all known to be operating on the principles of Psichiatria Democratica. It says much for the generosity of our Italian hosts that, despite what they perceived as criticisms of the reform movement, they were hospitable and friendly, allowing us free access to their services and discussing both practice and ideology at great length.

Trieste: the achievements

The Trieste services have been described in considerable detail by Bennett (1985). They operate basically through seven community psychiatric centres in different parts of the city and district, and we were able to visit five of these. The relationships between staff and patients (called 'users') are warm and caring; there are no white coats, no appointments, and no queues of patients waiting to be seen. The atmosphere is more like that of a club than a medical centre. In the centres in the city, patients come when they like, talk to whom they like, stay as long as they like, and leave when they like. Some treat the centres as lunch clubs, some come seeking the help of the staff (psychiatrists and nurses, with a psychologist and a social worker), and some work there, part-time or full-time, helping with the cooking and cleaning. This is not the traditional kind of patient labour, which is considered exploitative: there are cooking, cleaning, and agricultural co-operatives, which patients join; by an arrangement with the trades unions in the city, these pay full union rates. The health district budget provides the money on contract if the co-operatives tender is accepted.

There is no great distinction between staff and 'users'. Everybody is on first-name terms, and dress is informal. The presence of volunteers, some from other countries, helps to foster a sense of community. The main event of the day is the group meeting, when a variety of problems relating to individual patients or to relationships within the centre are talked out; but many other discussions go on between staff and patients, staff and volunteers, volunteers and patients, patients and patients.

Some patients live in their own homes, while others live in group flats near particular centres. These vary from small homely apartments, usually rented from the municipality, where patients have their own possessions and live a comfortable domestic existence, to large apartments which are very similar to hospital wards. In the former type, nurses come in regularly to supervise shopping, cooking, and cleaning, and to check on medication. The large apartments, for patients with limited degrees of independent functioning, tend to have full-time nursing staff. The nurses we met were young, cheerful, and had no formal training, though they had mental hospital experience; the patients greeted them as friends. They were more than home helps or care assistants, because they were capable of monitoring the patients' progress and reporting back to the psychiatrist. Psychiatrists visited the group apartments, and the degree of lateral support which they and the nurses had created between patients was impressive. We were told of cases in which quite acute psychotic episodes had been contained by doctors, nurses, and flatmates working together, without recourse to hospitalisation.

The City's Diagnosis and Cure unit in the general hospital has only eight beds. When we visited, all were empty—a great contrast to the crowded D and C units we had seen in other cities, where staff worked desperately with urban crises on locked wards, and patients could stay for months because there was nowhere else to send them. The consultant in charge thought that it was possible to run a service—even for the kind of 'heavy psychiatry' which came his way—without the use of mental hospital beds. Patients are usually kept in the unit only for a few hours, before being referred to a centre. Each of the centres has between six and eight back-up beds, and their psychiatrists work three or four shifts a month in the D and C unit, to keep in touch with the general hospital services. Most new referrals come in from the Casualty Department and the D and C unit; we were told that GP referrals to the psychiatric services are comparatively rare.

There is thus a network which begins with the D and C unit, acting as a crisis centre, extends to the mental health centres, and then spreads out into the apartments and patients' own homes, offering varying degrees of care and treatment. ECT is not used, and the use of medication appears to be less than in some other parts of Italy. The system is by no means as casual and informal as it looks on first examination, and as the psychiatrist at the D and C unit commented, the personal cost of involvement for the staff is high—perhaps higher than in more orthodox systems run on the medical model.

San Giovanni, the old mental hospital, was officially closed in 1980, to the accompaniment of public celebrations, but in fact, it is still very much open, though its use has been diversified. The hospital is built on a pleasant wooded site, on the villa system, and now houses the administration of psychiatric services, one of the seven centres, the co-operatives, the Arts Centre and a number of apartments for ex-patients. One of our critics (Ramon, 1985) complained that we did not understand the importance of 1968 in the work of

Psichiatria Democratica—the year in which left-wing students and workers combined in marches and demonstrations to try to bring about a more democratic society. We can only say that the spirit of 1968 is still very much alive in Trieste, and San Giovanni is its home. A block of patients' apartments (formerly doctors' flats) is labelled 'Casa Rosa Luxembourg'. A roughly-painted inscription along one wall reads 'Prison = asile = usine = école', a slogan left by a visiting group of French Communist students, expressing the Foucauldian principle that prisons, mental hospitals, factories, and schools are all agencies of capitalist control (Foucault, 1975; Jones & Fowles, 1984). Bearded young men play guitars, and sing "Blowing in the Wind", which must still be Trieste's most popular song, and talk of 'power to the people'. There are no punks, and we were asked on several occasions what Britain intended to do about 'the punk problem'. There is a sense in which it is still 1968 in San Giovanni.

It seems no accident that 'graffiti' is an Italian word: the walls of the San Giovanni villas express a natural delight in slogans, cartoons, and symbols. On Q ward, now empty, someone noticed that the letter Q looks like a child's drawing of a cat, and added ears. In successive pictures, the Q-cat stirs, stretches, and pads away to freedom. There are pictures of Marco, the horse made of wooden struts and plaster, who was pushed through the gates and surrounded by a ring of dancing children: when the hospital was symbolically closed in 1980; not a Trojan horse, as one commentator thought (Heptinstall, 1984), but a model of a real and much-loved horse which pulled the laundry cart collecting dirty sheets from the wards.

There is a special sense of carnival—Trieste is not far from Venice—expressed in the making of fantastic masks and posters, in dramatic entertainments and jazz concerts and happenings. San Giovanni is livelier than many a university campus, and a long way from the realities of mental hospital life in most of Italy. At the cost of possibly being dubbed 'anecdotal' or 'unscientific', we have tried to set it down as we experienced it. It is, above all, an *experience*—not to be described in terms of bed-days and clinic attendances and staff man-hours.

Trieste: the reservations

Like other visitors, we were attracted by this system (while continuing to point out that it was quite unlike the services we had encountered elsewhere in Italy: some of these had the enthusiasm, but did not have the resources). However, we had four major reservations, and it is necessary to set these down.

First, San Giovanni is not closed in anything but a symbolic sense. In addition to the 'Arts people', the co-operatives, the centre and the administration, it houses:

(i) over 200 patients who 'just happened' to be there when the reforms took effect and could not find outside accommodation. As in the community services, some of these are in small, personalised flats; but the degree of nursing support is greater, and some 'apartments' for very deteriorated patients, are simply hospital wards under another name. A locked ward for 48 patients suffering from senile dementia was particularly restrictive and unsuitable.
(ii) 15 beds in an alcoholic unit.
(iii) 20 beds for severely mentally handicapped young people, some of whom were lying on the stone floor of a balcony behind a locked door.
(iv) 40 beds in a traditional university clinic.
(v) an unknown number of beds in a hostel where patients attending the drug clinic (some of them volunteers in the Arts Centre), homeless ex-patients, and foreign students stayed.

To these categories can be added:

(vi) approximately 50 beds in the centres.
(vii) eight beds in the D and C unit.
(viii) perhaps one-third to one-half of the beds in the 100-bed *Allogia Popolare,* the city's public lodging-house, where a regular psychiatric clinic was maintained until recently.
(ix) an unknown number of beds in *convenzionati*—private nursing homes taking patients on contract from the public services, to which many patients over the age of 65 have been transferred. It is frequently said that "there are no *convenzionati* in Trieste". This is only correct if the cut-off point is taken as 65.

The total of all these beds cannot be far off that of a medium-sized mental hospital. Not all are considered the responsibility of the psychiatric services (for example, the drug clinic and the alcohol clinic are separately administered), but this is a matter of drawing administrative boundaries rather than of psychiatric need or social reality.

Second, we were concerned about the scope of the service. The emphasis is very much on the younger, psychotic patients, and on the containment of bizarre episodes. We appreciated Bennett's apprehension (1985) that the centres, while geared to the needs of such patients, might "overlook the needs of quietly deteriorating patients". A system which relies on emergency admission, self-referral, and word of mouth rather than on systematic case-recording may not fully meet the needs of patients suffering from depression, anxiety states, or long-term psychoses.

Third, the service appears not to provide for the elderly senile mentally ill, unless they had been in hospital before 1980, in which case they are regarded as victims of institutional oppression. It is assumed that, with the demise of the mental hospital, these patients will die off in time and not be replaced; but Trieste has an ageing population. Over 30% of its inhabitants are over the age of 65 (Gianichedda, 1985), and a system which virtually excludes them from psychiatric care seems, to put it mildly, unduly optimistic.

Fourth, it is important to note what the Trieste services do *not* do, in terms of professional practice. As elsewhere in the Italian psychiatric services, there are no regular programmed therapeutic activities. A volunteer who attempted to keep a diary of activities in one of the centres gave up, because there were no activities apart from discussions and the work of the co-operatives. In the past, patients have been exploited and used as an unpaid labour force, so that this reaction is understandable; but some patients could benefit from the kinds of occupational therapy, educational classes, health and beauty classes, and other activities which are standard in many British day hospitals and centres. Patients should not be compelled to join in such activities, but perhaps they should have the choice, since many of them lack the initiative to structure their own day. (On the other hand, we are aware that the differences between Italian and British practice could relate to cultural norms rather than to psychiatric norms. Perhaps our emphasis on activity is the result of living in a colder climate.)

The discussions in the centres on patients' needs were practical and relevant in everyday terms, but there seems to be no use of psychoanalytic insights (which are considered bourgeois), group therapy techniques (which are thought to be manipulative), or any of the modern developments in social work, such as family therapy, the systems approach, or network theory. Specialists in any of these areas would find the Trieste system low-powered—its real power lies elsewhere. There is no systematic case-recording, no performance review, no outside monitoring, no staff development system, and no systematic training. Whilst recognising that these devices may become mechanical and take the place of human concern, there is an argument for having some elements of both.

Finally, behind the innocent and frolic radicalism, there are more serious political implications. We did not wish to enter into ideological debate, but most issues in Italian life are highly politicised, and we were repeatedly told that it was impossible to divorce the practice from the ideology. The principles, as far as we could elucidate them, are as follows: the mental hospital system is an expression of capitalist oppression of the workers. Therefore 'the closure of the mental hospital is the point of departure'; the people must rise up and demand that mental hospitals be closed. Doubtless some patients will suffer in the transition period, but 'it is necessary to take risks'. Eventually, the people will rise up and demand good community services, but the real aim is 'the transformation of Italy'. What has been done in Trieste can be done elsewhere—all that is necessary is that "psychiatry should deinstitutionalise itself".

The same phrases were used so frequently in discussion that we came to the conclusion that this was a closed system of thought, insusceptible to rational argument. We pointed out that the mental hospital was not closed, and that the Trieste system might carry very much more weight in international circles if the psychiatrists concentrated on publishing research results on the positive aspects of the service, rather than creating a credibility gap with slogans and doctrinaire statements. The reply was "You do not have the correct frame of reference": all that is necessary is to be ideologically sound—and to close the mental hospital.

The Trieste experience appeals to the non-rational side of the human mind. Demands for liberty, equality, and fraternity still create resonances and enthusiasms, powerfully reinforced by symbols and slogans of a highly imaginative kind. But three points stand out: first, the demand is for total acceptance; analysis and questioning are swept aside or treated as evidence of adherence to 'the medical model' or extreme Right-wing politics. There are also rigidities of thought on the Left. Second, in a country with a Catholic heritage, symbols and dogma still have a considerable power. Third, both have a new impact through the mass media; Psichiatria Democratica's use of the media has been highly professional.

Can the Trieste experience be replicated?

The insistence that what has happened in Trieste can be replicated anywhere else is worth further examination. The Trieste psychiatric services have certain built-in advantages. The district is discrete in geographical and administrative terms—a promontory largely bounded by the Adriatic and the mountains. It comprises a single health district, which means that it is possible to plan services for the district as a whole. By contrast, Milan has 19 health districts, and Rome has 20, each with its own health budget. In Trieste, one-to-one relationships between the psychiatric services on the one hand and the commune, local trades unions, and related agencies on the other are possible, as they are not in most cities; administrative complexity makes community care difficult. The movement started at a propitious point in time, and with a charismatic leader, Professor Franco Basaglia, who generated enthusiasms and gained much popular support. The Region supports the service well—in terms of population served, the annual budget is at least four times as high as that of some psychiatric services in Rome. One point which is generally overlooked is that a 'core and cluster' system involving group flats needs an adequate supply of housing: Trieste has a declining population, which means that there are apartments to spare at relatively low rents. Gianichedda (1985) records a steady decline, involving both natural and migratory shift, of over 20 000 (about 7%) over the 20 years from 1961 to 1982; as a result, "the decrease in population has left many houses empty and these are now unlet. The official figure shows 27,860 empty rooms".

Elsewhere in Italy, it is more difficult to implement the principles of Psichiatria Democratica. In Ferrara, though there is an insistence on the importance of symbolically closing the mental hospital (the *primario* has personally painted a large crack in one wall, and expects to have the main gate ceremonially demolished next spring), there are still 200 or more patients in the old hospital, for whom rehabilitation seems remote, and a further 120 in a converted convent about two miles out of the city. A disused part of the hospital is being converted into flats by the health district, but the psychiatric service will only be able to control the use of four. Long-stay patients who have left the hospital have either returned to their own homes or have gone to live in the former Jewish ghetto—a poor part of the city: "They are tolerated there", we were told.

The Ferrara team has a strong psychoanalytical orientation, and works through out-patient clinics (with appointments and individual interviews); their work focuses on patients with a diagnosis of depression or anxiety state. There are no clubs or day centres. The elderly confused and the quiet schizophrenic are regarded as the responsibility of the Social Services, and violent or dangerous patients as the responsibility of the forensic hospitals. The team does not deal with drug or alcohol abuse, and takes the view that the problems of young people are best dealt with by family therapy. When asked how they would spend additional finance, if it were available, the psychiatrists opted for professional training—for psychiatrists, for social workers, and above all for nurses. Though the ideology was similar to that in Trieste, the practice was fundamentally different. The psychiatrists were primarily interested in the *casa interna*, the house of the mind, rather than the *casa externa*, a house for the patient to live in.

In Bologna, which has three health districts, we visited one where the *primario* subscribed to the principles of Psichiatria Democratica, but took the view that only national mental health planning would enable Law 180 to work as it should. He was responsible for a total of 290 beds, many of them occupied by chronic patients and all run on orthodox medical lines, with one locked ward. The community services consisted of an outpatient clinic and some domiciliary work by community psychiatric nurses.

In Rome, we were able to talk to three University Professors of Psychiatry, all with a responsibility for running services; all three are members of the Italian Communist Party. Two are members of Psichiatria Democratica, but one has left the organisation because he thinks it is becoming dated; he took the view that it was insufficiently in touch with recent developments in psychopharmacology and community medicine.

Of the 20 health districts in Rome, one informant rated three or four as good, five or six as 'medium—improving', and the rest as poor. There are two large mental hospitals, and only 45 Diagnosis and Cure beds; the pressure on services is extremely acute. There are few psychologists or social workers available, and few if any group flats—Rome has a housing shortage.

One professor thought that if he had sufficient resources, he could set up a service on Trieste lines; he attributed the main problems in applying Law 180 to the misapplication of funds. Of the money available for psychiatric services in the Region, roughly half goes to private Homes (*convenzionati*) and private psychiatric hospitals. Public mental hospitals take up nearly another quarter, and the whole of the community services in 20 districts run on the equivalent of £14 million a year.

Another professor, in a very poor district of Rome with acute social problems, said of Trieste "that model cannot be reproduced", and that if he had sufficient funds to develop the psychiatric services, he would prefer to spend it on more fundamental needs in the community: homes, schools, getting rid of squatters' houses. "The people here don't live—they survive".

All three were in favour of an eclectic approach to patients' problems: psychopharmacology, group and individual therapy, social therapy, and community support. We were able to visit centres in Rome—notably the Albedo Centre and the Random Centre—where advanced training takes place for doctors and other professionals. The emphasis is on multi-disciplinary work of a high professional standard including both medical and psychoanalytical techniques.

Conclusions

"Trieste is a flag" said one professor. It seems that the Trieste services, which rely so heavily on symbols for their impact, have in turn become a symbol—of humanitarian concern for patients' welfare, perhaps of nostalgia for a period in time when the 'transformation' of Italy' seemed politically possible. Today, elsewhere in Italy, Psichiatria Democratica seems to be diversifying, coming to terms with adverse administrative situations, and accepting new developments in medicine and the social sciences. It was significant that when we asked a group of psychiatrists in Trieste why, if this 'transformation' was merely a matter of 'deinstitutionalising psychiatry', they did not move and tackle the problems elsewhere in Italy, the response was "But the administration would be against us". Perhaps it is also significant that, in the last two years of his life, Franco Basaglia moved to Rome, where he took on the administration of psychiatric services for the whole of the Lazio Region, i.e. the city and the surrounding area. Basaglia was a man of extraordinary courage.

For much of our time in Italy, we remained mystified by the insistence of Psichiatria Democratica on 'closing the mental hospital' when it was patently obvious that mental hospitals were not being closed. As in other countries, which do not employ the same rhetoric, their populations have been reduced, and some community services have been developed. In Trieste, the community has been brought into the hospital and the hospital services into the community in a unique way which blurs the distinction between the two; but changes of nomenclature and the re-drawing of administrative boundaries do not dispose of the problems of patients, and the danger that the needs of chronic patients might be overlooked seemed to us a real one.

It was possible that 'closing the mental hospital' was no more than a slogan for public consumption—a latter-day equivalent to razing the Bastille—and that Psichiatria Democratica was well aware that it did not correspond to the reality. However, we did not think that this was the case; despite our ideological differences, we never doubted their good faith or their complete sincerity.

A second possibility was that this was the equivalent of 'gate fever'—a condition well-known in prisons and concentration camps, in which the actual breaking down of the gate becomes more important than a consideration of what life is like on the other side. Before the 1970s, many Italian mental hospitals were, by all accounts, uncommonly repressive. There was nothing equivalent to the British movement for voluntary treatment under the 1930 Mental Treatment Act or informal treatment under the 1959 Mental Health Act, or the open door movement of the 1950s. In the circumstances, 'gate fever' would be understandable, but typically, the symbol comes adrift from reality.

There is a third, more sociological explanation. In common parlance, a prison or a mental hospital is merely a building, a physical landmark; but in Marxist sociology, which has been very influential in Trieste, it is also a power-structure, constraining and controlling the inmates. So San Giovanni is 'closed' in the sense that the hospital administration ceased to exert power over the inmates, but it is not 'closed' in the sense that some of them continue to live there and to receive psychiatric and nursing services. The distinction is not a particularly subtle one, but it has led to massive misunderstandings. When the Trieste team say "We closed the mental hospital", they do not mean "We closed the mental hospital", They mean "We broke the power of the mental hospital over the patients".

We do not claim to have seen the whole of Italy, nor to be able to make detailed and authoritative comparisons of specific issues; but we know enough to be able to state with confidence that the more extreme claims made for 'the Italian Experience' have been highly misleading. There is now a growing literature on the subject in English, including the symposia published recently by the *International Journal of Mental Health* (Mollica, 1985) and *Acta Psychiatrica Scandinavica* (Perris & Kemali, 1985). We hope that readers will be able to study this literature, and make up their own minds.

Notes on correspondence

Shulamit Ramon (1985) mentions 12 political proposals for the reform of Law 180, which come from all the major political parties except the Communist Party. The proposals of the Government, the Christian Democrats, the Liberals, and the Republicans, which we have analysed, all provide for "units for protracted hospitalisation", "protracted stay units", or the "restructuring" of mental hospital accommodation to provide for chronic patients. We did not at any time compare Franco Basaglia to Winston Churchill.

Tansella (1985) evidently missed the reference and the footnote in our first paper to the longer and more descriptive account (Jones & Poletti, 1985b), which describes in some detail the rationale of our investigation, the research design, and the places visited. We did not publish the names of our informants, and have not done so in the present paper, because we had many enquiries from readers wishing to visit the Italian services and we thought that our sources should be protected. Many of the doctors and other professionals who were kind enough to spare us time were working under great pressure. Of the sources which Tansella quotes, we were familiar with most published up to and including 1984, but the Scala & Gritti (1985) paper, was published after our own went to press.

In Jones & Poletti (1985b), we distinguished very clearly between those Italians who believe Law 180 is a good law which failed in implementation, and those who believe that it is a bad law. Doubtless this debate will continue.

De Girolamo (1985) states that "compulsory admission is easily implemented in case of need"; that may be the case in Cremona, but is not so in Rome, where there are 45 D & C beds for a population of five million. The Law specifies 15 beds for 150,000 population, but many areas are still below this level of provision.

Discussions about the statistics for *convenzionati* or suicides are not useful because the data are unreliable. Some figures of *convenzionati* certainly exclude the over-65s, or patients placed in general, rather than psychiatric nursing homes, while numbers of suicides are notoriously difficult to assess, particularly in Catholic countries. We have no figures for forensic hospitals, but understand that these are given in terms of bed-days, not of patients resident or admissions/discharges. It is true that the Trieste service does not make a practice of sending patients to forensic hospitals: we were told that the practice is to keep them in the local prison, where they can be visited by a psychiatrist from one of the centres with a view to their ultimate rehabilitation.

Bourne (1985) asks whether we attended the Psichiatria Democratica exhibition in Sheffield last year: we were in Italy at the time. He also asks whether it can really be true that "we can learn nothing from the Italian experience": we learned a great deal about Italy, but do not think that the solutions of Trieste are transferable to a British context.

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*Kathleen Jones, BA, PhD, HonFRCPsych, *Professor of Social Policy, University of York, Heslington, York YO1 5DD.*

Alison Poletti, BA, *Research Student, 52 Carmel Street, Belfast, BT7 1QU.*

*Correspondence

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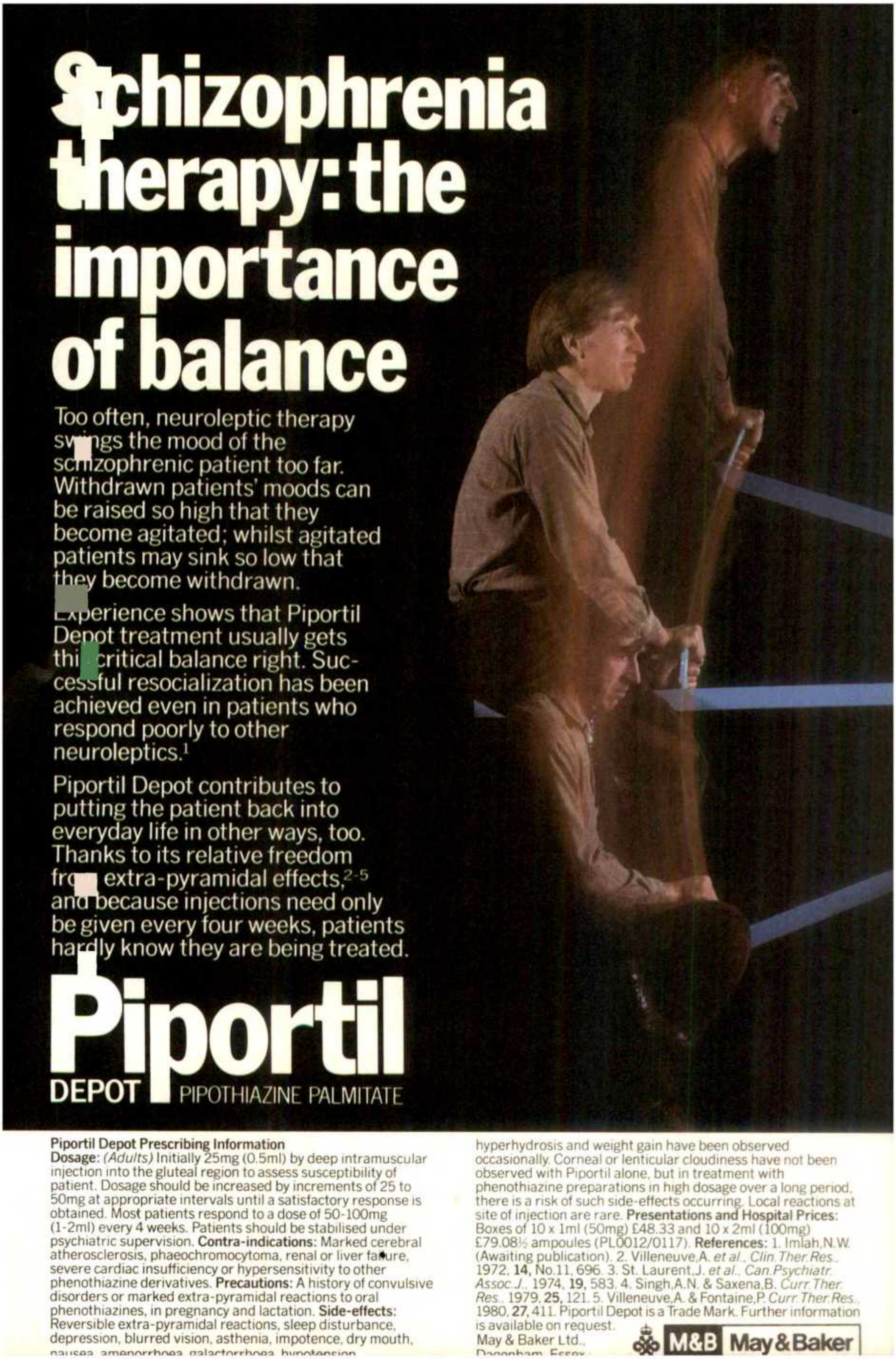

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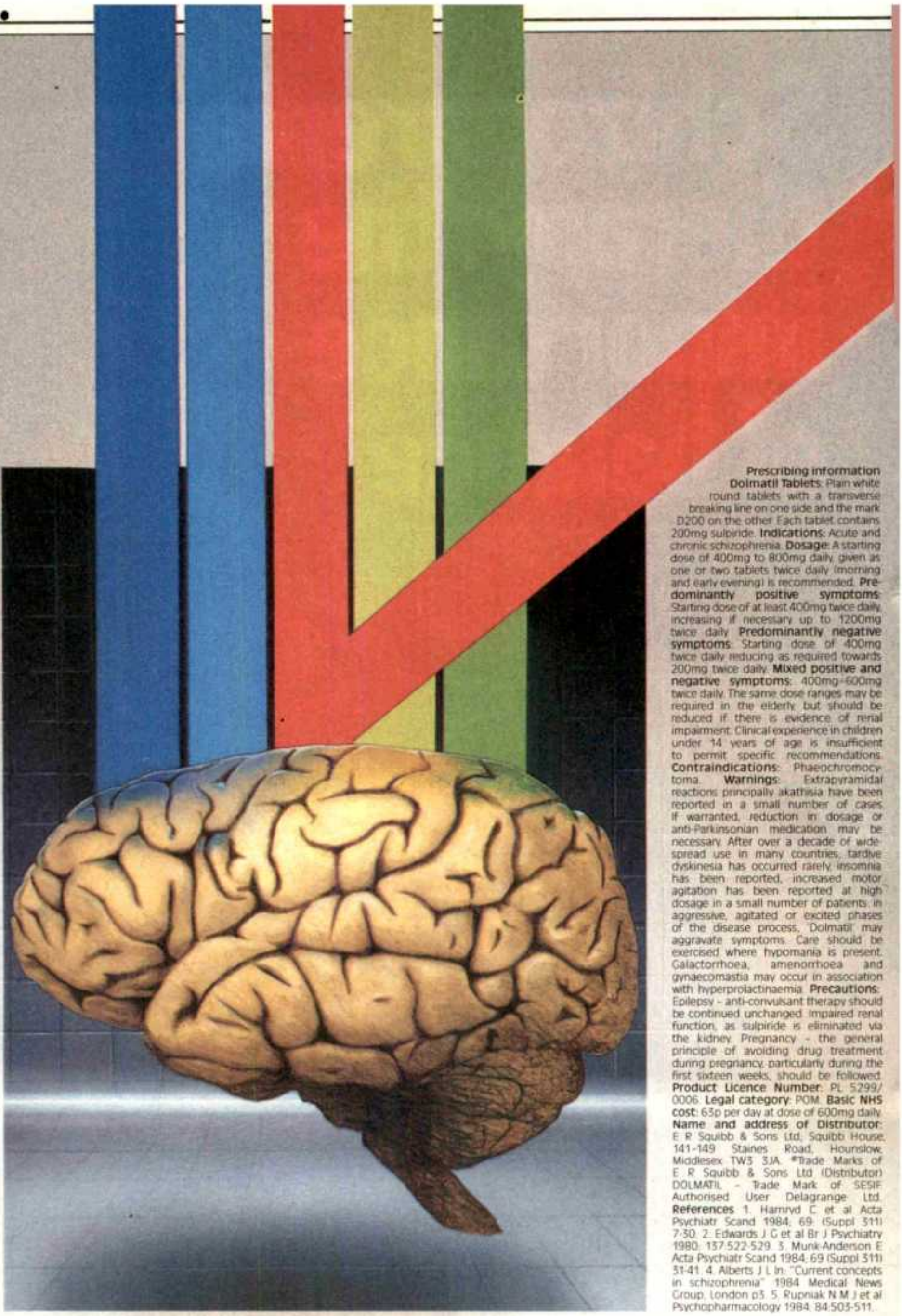

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This low incidence of tardive dyskinesia with Dolmatil may be explained by the absence of an increase in brain D_2 receptor numbers (the basis of 'supersensitivity' phenomena) after chronic administration to animals[5]

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Dolmatil Tablets: Plain white round tablets with a transverse breaking line on one side and the mark D200 on the other. Each tablet contains 200mg sulpiride. **Indications**: Acute and chronic schizophrenia. **Dosage**: A starting dose of 400mg to 800mg daily, given as one or two tablets twice daily (morning and early evening) is recommended. **Predominantly positive symptoms**: Starting dose of at least 400mg twice daily, increasing if necessary up to 1200mg twice daily. **Predominantly negative symptoms**: Starting dose of 400mg twice daily reducing as required towards 200mg twice daily. **Mixed positive and negative symptoms**: 400mg–600mg twice daily. The same dose ranges may be required in the elderly, but should be reduced if there is evidence of renal impairment. Clinical experience in children under 14 years of age is insufficient to permit specific recommendations. **Contraindications**: Phaeochromocytoma. **Warnings**: Extrapyramidal reactions principally akathisia have been reported in a small number of cases. If warranted, reduction in dosage or anti-Parkinsonian medication may be necessary. After over a decade of widespread use in many countries, tardive dyskinesia has occurred rarely. Insomnia has been reported, increased motor agitation has been reported at high dosage in a small number of patients. In aggressive, agitated or excited phases of the disease process, 'Dolmatil' may aggravate symptoms. Care should be exercised where hypomania is present. Galactorrhoea, amenorrhoea and gynaecomastia may occur in association with hyperprolactinaemia. **Precautions**: Epilepsy - anti-convulsant therapy should be continued unchanged. Impaired renal function, as sulpiride is eliminated via the kidney. Pregnancy - the general principle of avoiding drug treatment during pregnancy, particularly during the first sixteen weeks, should be followed. **Product Licence Number**: PL 5299/0006. **Legal category**: POM. **Basic NHS cost**: 63p per day at dose of 600mg daily. **Name and address of Distributor**: E R Squibb & Sons Ltd, Squibb House, 141-149 Staines Road, Hounslow, Middlesex TW3 3JA. *Trade Marks of E R Squibb & Sons Ltd (Distributor) DOLMATIL - Trade Mark of SESIF Authorised User Delagrange Ltd. **References** 1. Harnryd C et al Acta Psychiatr Scand 1984; 69 (Suppl 311) 7-30. 2. Edwards J G et al Br J Psychiatry 1980; 137:522-529. 3. Munk-Anderson E Acta Psychiatr Scand 1984; 69 (Suppl 311) 31-41. 4. Alberts J L In: "Current concepts in schizophrenia" 1984 Medical News Group, London p3. 5. Rupniak N M J et al Psychopharmacology 1984; 84:503-511.

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The General Hospital Psychiatrist: Too Many Tasks and Too Few Roles?

TOM SENSKY

What should the general hospital psychiatrist do, and how should he do it? In psychiatric settings, psychiatrists may legitimately confine their attention to those patients whose disorders can be classified according to ICD-9, but in general hospital settings, the same approach defines a very restricted range of activities. Evidence is reviewed which highlights the differences between psychiatric disorders encountered in psychiatric hospitals and those found in primary care or general hospital settings. Different activities proposed for the general hospital psychiatrist, and the results of research comparing these, are reviewed. A recent study is discussed in which alteration of the psychiatrist's method of practice in a general medical unit produced considerable changes in the pattern of psychiatric referrals. Evaluation of the efficacy of their interventions should remain the ultimate goal of general hospital psychiatrists. This can be adequately undertaken only by means of better understanding of the process by which general hospital patients attract psychiatric referral.

General hospital psychiatry involves collaboration between psychiatrists and others working in the general hospital in the detection and management of psychiatric morbidity. Although clinical work, research and teaching are equally important facets of the general hospital psychiatrist's work, only the clinical aspects of general hospital psychiatry will be considered here. Many general hospital psychiatrists work in specialised settings like cardiology or oncology units, but attention will be focussed on the work of the psychiatrist in general medical and surgical wards where the problems of defining roles and tasks are most conspicuous.

Definitions

The term *general hospital psychiatry* is preferable to *liaison* or *consultation* psychiatry. These latter terms are only sources of confusion. Liaison is practiced in primary care settings as well as in general hospital settings. Although these two activities have many common features (see below), the distinction between them is justified because general hospital psychiatry also involves particular problems of its own. Furthermore, although *consultation* has a similar meaning in psychiatry and in other medical specialities, what psychiatrists refer to as *liaison* is described by those other non-medical professionals with whom they work as *consultation*.

For the purposes of this paper, *role* is intended to refer to the activities and attitudes expected of the psychiatrist (Hawkins, 1958; Tuckett, 1976). Task describes what he actually does or attempts to do and more particularly, how he goes about his work.

Roles

The general hospital psychiatrist's role can be viewed from numerous perspectives, which may differ considerably from one another (Noy *et al*, 1966). Of these, two in particular will be contrasted, namely the perspective of the psychiatrist himself and that of the doctor making the psychiatric referral.

The physician expects the psychiatrist to be interested in emotion, personality and distress. Physicians are unlikely to be as interested as some psychiatrists might be in distinguishing "distress" from "disorder". For almost all British psychiatrists who see referrals from medical or surgical wards, this activity will constitute only a minor part of their work, most of which will be based in psychiatric units or hospitals. Seeing psychiatric disorders from the vantage point of the psychiatric hospital, psychiatrists might expect to confine their work in general hospitals to the same range of problems they encounter among their psychiatric in-patients. However, bearing in mind that most psychiatric morbidity exists outside psychiatric hospitals, this offers a biased perspective of psychiatry based on a

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highly selective population of patients. The psychiatrist's practice in managing his in-patients bears little relationship to his roles elsewhere, particularly in the community or in primary care settings (Williams *et al*, 1980).

Another potential difference between psychiatrist and referring clinician, often quoted in the American literature but probably less important in the U.K., is the expected focus of the psychiatrist's intervention. Physicians generally expect their psychiatrist colleagues to be *consultants* (in the sense used by doctors), focussing on the patient and his problems rather than on staff conflicts and ward dynamics (Karasu *et al*, 1977; Sasser & Kinzie, 1978; Ochitill, 1983).

At least in the U.K., the decision to refer a patient for psychiatric assessment commonly rests with the senior doctor under whose care the patient is admitted to hospital. In making this decision, it is the referring clinician and not the psychiatrist who first defines a problem as "potentially psychiatric". For this reason, it is unhelpful for the psychiatrist simply to redefine the referral as inappropriate, any more than a surgeon would class as inappropriate being asked an opinion on a patient with a suspected acute abdomen whom he declines to take to theatre. This also emphasises the need for the psychiatrist to consider in his assessment not only the patient's problems but also the reasons for referral. However, there is probably a difference here between primary care and general hospital settings. A proportion of patients attending a general practice surgery will request psychiatric referral and a further percentage can be prepared for this by the general practitioner over time. It is probably less common for patients to seek and successfully negotiate admission to an acute medical ward with the intention of seeing a psychiatrist.

Similarities between psychiatry in primary care and general hospital settings

The work of psychiatrists in primary care settings is acknowledged to be very different from the management of psychiatric inpatients. The extent to which practice in either of these settings resembles psychiatry in general hospitals might help in attempting to define the general hospital psychiatrist's roles.

Consider, for example, the psychiatric diagnoses given to general hospital inpatients referred to psychiatrists. Studies from the U.S.A. and Britain reveal a consistently low percentage of referrals diagnosed as schizophrenic. In most studies, a far greater proportion of referrals are given the diagnosis of personality disorder [Table I]. The same pattern emerges from several studies of new psychiatric outpatient attenders referred by general practitioners. For example, in Johnson's (1973) study of a series of consecutive new referrals, 29% were diagnosed as having a personality disorder and only 4% given the diagnosis of schizophrenia. In the same year, schizophrenics constituted 18% of total psychiatric inpatient admissions in England and Wales, while personality disorders accounted for 10% of total admissions (DHSS, 1976). It is important to note that these figures do not accurately reflect prevalence, but represent the complex interaction of numerous factors, including (amongst others) the decision by doctors to refer patients.

Psychiatric disturbance in general hospitals tends to be short-lived (Shepherd *et al*, 1960; Kenyon & Rutter, 1963). Once again, this contrasts with the disorders of many psychiatric *in-patients*, but resembles psychiatric morbidity diagnosed in primary care settings (Kedward, 1969; Kaeser & Cooper, 1971). Allied to this, there is a striking (and perhaps surprising) consistency in psychiatric follow-up of

TABLE I

Psychiatric diagnoses of general hospital in-patients referred for psychiatric assessment

Study	*% Total referrals*	
	Schizophrenia	*Personality disorder*
Shepherd *et al* (1960)	2.2	32.1
Kenyon & Rutter (1963)	3.8	24.8
Bridges *et al* (1966)	2.1	21.7
Crisp (1968)	2.9	2.6
Kligerman & McKegney (1971)	—	25.4
Anstee (1972)	5.5	11.8
Shevitz *et al* (1976)	0.3	—
Torem *et al* (1979)	5.0	16.3

TABLE II

Follow-up of general hospital in-patients referred for psychiatric assessment

Study	*% Total referrals*	
	Seen once only	*Transfer to psychiatric bed*
Fleminger & Mallett (1962)	31	22
Kenyon & Rutter (1963)	34	19
Bridges *et al*, (1966)	35	10
Crisp (1968)	35	17
Anstee (1972)	33	28
Thomas (1983)	21	16
Sensky *et al*, (1985) [Method I]	23	11
[Method II]	31	8

referrals from general hospitals (Sensky, 1985). In most studies, about one-third of referrals are seen once only for assessment and 10–20% warrant transfer to a psychiatric bed [Table II]. Very similar figures to these have been reported for patients referred by general practitioners to psychiatric outpatient clinics (Kessel *et al*, 1965; Kaeser & Cooper, 1971; Johnson, 1973).

Particular features of psychiatric problems in general hospitals

There are two other features shared by general hospital in-patients which set them apart, as a group, from other populations in which psychiatric morbidity is investigated and treated. Firstly, most of them have some physical illness which may or not be related to their psychiatric disturbance and secondly, they have all experienced the same recent life event, namely hospitalisation, and all that this implies. For such in-patients, defence mechanisms and coping strategies become particularly important, and the assessment and understanding of these should be incorporated into the general hospital psychiatrist's role. Consider, for example, a man in his 50's forced into premature retirement after developing a lymphoma that had not responded to treatment. Psychiatric referral followed the observation of the ward staff that, although he appeared very stoical about his illness, both he and his wife were very distressed and in tears whenever she visited him in hospital. The staff had found out that his wife was receiving antidepressants from her general practitioner. This man was very angry that he was referred to a psychiatrist because he wished to say nothing about his condition but rather to remain what he termed a "fatalist". He was attempting to cope with his poor prognosis by denial while his wife felt the need to share her distress with her husband, as she had always done in the past. The importance of this problem to the psychiatrist lies in the observation that the use of denial by patients with some cancers may lead to a more favourable prognosis, at least as measured by short-term outcome (Greer, *et al*, 1979), whereas for a spouse, such denial may hinder preparation for bereavement (Parkes, 1972).

There are other kinds of problem that present more frequently in general hospitals than elsewhere. A man in his 40's had been unable to work for some years because of a recurrent fear that he was about to suffer a myocardial infarction. He presented in Casualty at frequent intervals pressing for further investigations, sometimes having been brought there by ambulance. His insatiable demands for reassurance had led him to fall out with one general practitioner after another. He frequently telephoned his wife at work (she was the only breadwinner in the family), insisting she return home immediately because he was about to die. His wife persistently refused to be interviewed or to involve herself in any other way in her husband's management. His two eldest children had been sent away to boarding school and the third child later set fire to her school. All psychiatric interventions that had been attempted over the years had failed but at least his psychiatric outpatient appointments helped to set some limits, supporting his general practitioner and keeping him away from Casualty. Although this man warranted the diagnosis "personality disorder", this conveys little useful information about his presentation in the general hospital.

Problems of classification of psychiatric disturbance in general hospitals

Psychiatrists have been accustomed to seeing as their role the management of a group of disorders which can be designated as "psychiatric". In seeking positive reasons to take up referrals, psychiatrists are likely to resort to the use of familiar psychiatric classifications like ICD–9 (World Health Organization, 1978). This, like many of the operational and research diagnostic instruments in common use, was developed primarily among more severely ill psychiatric patients, particularly in-patients in psychiatric hospitals. ICD–9 has proved inadequate to meet the needs of psychiatrists working in primary care. The psychiatric problems encountered in general hospitals bear a much closer resemblance to those in primary care than those in psychiatric hospitals. In addition, there are some aspects of psychiatric illness which are much more common in general hospitals than elsewhere. For both these reasons, ICD–9 and similar classifications are of very limited use to general hospital psychiatrists, and those who define their roles in terms of ICD–9 can expect to have little to do, leaving many psychiatric problems unattended to.

Much of the general hospital psychiatrist's work is manifestly concerned with the *relationship* between physical and psychiatric disorder. Any classification which fails to take account of this must prove inadequate, but to the author's knowledge, there is no classification presently available which successfully meets this requirement. Moreover, it is important that, even if an ideal classification were available, this alone would not be adequate to define the psychiatrist's roles. Any classification of the disorders a psychiatrist actually sees, cannot alone address the observation that some patients attract psychiatric referral while others, who may equally warrant psychiatric assessment, are not referred. Once again, this highlights the need for the general hospital psychiatrist to concern himself with the circumstances of the referral and the reasons behind it.

Tasks

Perhaps as a result of the difficulties in defining the general hospital psychiatrist's roles, the tasks he can choose for himself appear almost limitless, prompting the view that there are as many forms of liaison as there are liaison psychiatrists. This is reminiscent of Professor Kessel's caution that "it may be that there is no form of social deviation in an individual which psychiatrists will not claim to treat or prevent—the pretensions of some psychiatrists are extreme" (Kessel, 1963). Lloyd (1980) has recently reminded general hospital psychiatrists of this pitfall, while Strain (1983) has defended general hospital psychiatry against similar criticism by Neill (1983).

The methods used by general hospital psychiatrists in their work can be divided into several broad categories. The *patient-oriented* approach is the most commonly used in Britain. Here, the psychiatrist's attention is confined to the patient, who has usually been referred by the consultant in charge of his care in hospital. The *consultee-oriented* method (Schiff & Pilot, 1959), is based on the work of Bibring (1956) and others. In this approach, the focus is shifted from the patient to the referring physician, the prime assumption being that referral reflects the physician's concerns as much as, if not more than, the patient's problems. The *situation-oriented* method (Greenberg, 1960) involves "the consultant psychiatrist as participant observer of what is essentially an on-going 'small group' in which the patient is the central character" (Meyer & Mendelson, 1961). All these methods, as well as an additional, "organization-oriented" approach, were outlined in 1954 by Caplan in his book on mental health consultation (Caplan, 1970).

Here also there are parallels between psychiatric practice in general hospitals and in primary care settings. In a recent investigation, the General Practice Research Unit at the Institute of Psychiatry found three basic approaches to collaboration between general practitioners and psychiatrists working in primary care settings (Strathdee & Williams, 1984). These three approaches correspond quite well to the methods cited here. It is particularly interesting that where collaboration between general practice and psychiatrist was longstanding, the approach which seemed to evolve most commonly was the situation-oriented one, focussed on the professionals rather than on increased direct involvement with patients.

Other methods are less common. Specialised "psychosomatic inpatient units" have been described (Kohle, 1983) in which the physicians undergo psychiatric or psychoanalytic training and strong emphasis is placed on the psychosocial aspects of illness. Another approach involves combined medical and psychiatric inpatient units (Molnar *et al*, 1985). A more extreme solution recently proposed by two American authors (both psychiatrists) is that the primary management of some physically ill patients should be taken out of the hands of physicians and entrusted to psychiatrists (Fogel & Goldberg, 1983).

Comparisons between methods of psychiatric practice in general hospitals

In practice, these methods (especially the common ones) tend to be used together, although psychiatrists will vary in their preference for one approach over the others. A psychiatrist might expect different referrals from a health centre if, instead of using it merely as a site for one of his outpatient clinics, he joined the general practitioners in regular Balint groups. In the same way, the referrals any general hospital psychiatrist can expect and the ways in which he deals with them are likely to be influenced by the method of practice he favours. Despite this, there is very little published research relating to the effects of different methods of general hospital psychiatric practice.

Crisp (1968) demonstrated a dramatic rise in referrals following the attachment of a psychiatrist to a particular medical unit. He also commented that referrals to this service from surgical firms decreased following the retirement of a particular surgeon. Pritchard (1972) carried out a retrospective study of patients given a psychiatric diagnosis on discharge from non-psychiatric wards at the London Hospital. He found that the eight general medical firms varied considerably in the proportion of their patients, excluding parasuicides, given a psychiatric diagnosis on discharge (between 1.9 and 6.5%). Among this group of patients given a psychiatric diagnosis on discharge, the percentage who had been referred for psychiatric assessment also varied according to firm, from 15 to 50%. Pritchard's data showed that the more patients a physician diagnosed as psychiatrically ill, the greater the percentage of these patients he referred for psychiatric assessment. More particularly, the more use a physician made of psychiatric referral, the more likely he was to refer his patients to a specified consultant. This underlines the importance not only of the physician's attitudes to psychiatry but also of the relationships established between psychiatrists and the other clinicians with whom they work.

Torem *et al* (1979) investigated two contrasting methods of psychiatric practice applied in a particular medical unit of one New York hospital. The psychiatrist's more active involvement on the unit led to a ten-fold increase in referrals and also to a change in the types of problem referred. A group of patients was identified for whom the physicians were reluctant to seek psychiatric assessment even though the psychiatrist considered referral warranted. Torem and his colleagues referred to this as "physician resistance to psychiatric referral" (Steinberg, *et al*, 1980), unfortunately ignoring the possibility that this apparent "resistance" could reflect difficulties in their own relationships with their physician colleagues. Patients in this group were finally seen after a senior psychiatrist had negotiated with the physicians to sanction their referral. More patients in this group than in any of the others received either no psychiatric diagnosis or had their diagnosis deferred, an interesting observation about which the authors offered no comment.

Other studies of different methods of psychiatric practice have involved specialised settings such as paediatric hospitals (Sack & Blocker, 1978) or the use of psychiatric nurses rather than psychiatrists (Davis & Nelson, 1980; Maguire *et al*, 1980; Lipowski & Wolston, 1981). Consideration of these studies is beyond the scope of this paper, although they are of great importance, particularly in the development of multidisciplinary approaches to psychiatric morbidity in general hospitals.

A teaching hospital study

We recently compared two different methods of psychiatry referral (Sensky *et al*, 1985). In the established method (Method I), patients were seen in response to a formal written request for consultation instigated by the consultant in charge of the patient's care. No attempt was made to liaise with staff directly involved in the patient's management beyond writing an assessment in the medical notes. The referrals seen by this method by one psychiatrist (myself) were compared with those by Method II, in which the same psychiatrist developed a link with one particular medical unit. This entailed regular attendance at weekly "social" rounds which had already been established on the firm, the establishment at the request of the nursing staff of a weekly staff support group (Sensky & Greenberg, 1985) and weekly teaching for the medical students on the firm. With the encourgement of the consultants on the firm, referrals were accepted not only from any of the doctors but also from other staff.

Use of method II resulted in qualitative as well as quantitative changes in referrals. Whereas method I produced a psychiatric referral rate of 2–3 per 100 inpatients discharged, this rose to 8 per 100 discharges when method II was adopted ($P<0.0005$, chi-square test). The referral rate for female patients (9.8 per 100 discharges) was higher than for males (7 per 100 discharges ($0.1 > P > 0.05$, chi-square test). The age distribution of the referrals by method II was similar to that of the inpatient population from which the referrals were drawn except that patients under 30 years old were overrepresented. It is probably significant that most of those *making* referrals fell into the same age group. The distribution of problem types differed significantly between the two methods and for method II there were also significant differences between male and female referrals in this respect [Fig. 1]. Overall, the most common problem among method I referrals was coincidental psychiatric illness, although for male referrals by this method, the single most common presenting problem type was some somatic complication of psychiatric disorder (mainly alcoholism). The most common type of problem referred by method II was the somatic presentation of psychiatric disorder (mainly pain and other somatic symptoms for which no organic cause had been found). Psychological reactions to physical illness (such as extreme denial or depressive reactions) were commonly referred by both methods. Neither method resulted in the referral of any patients with psychosomatic disorders, defined as physical illnesses in which psychological factors were considered to be of major aetiological importance. This agrees with the findings of others that such problems seldom come to light outside specialist centres (Crisp, 1968; Torem, *et al*, 1979; Thomas, 1983).

Despite the much higher referral rate by method II, a similar proportion of patients from both referral sources were offered psychiatric follow-up after discharge from hospital. This indicates that the change in the psychiatrist's method of working led to the referral of three times as many patients as before who warranted his intervention. It also argues against the difference between referrals by these two methods being due to a lowered threshold for referral by method II because of easier access to psychiatric help. In the group of patients referred by

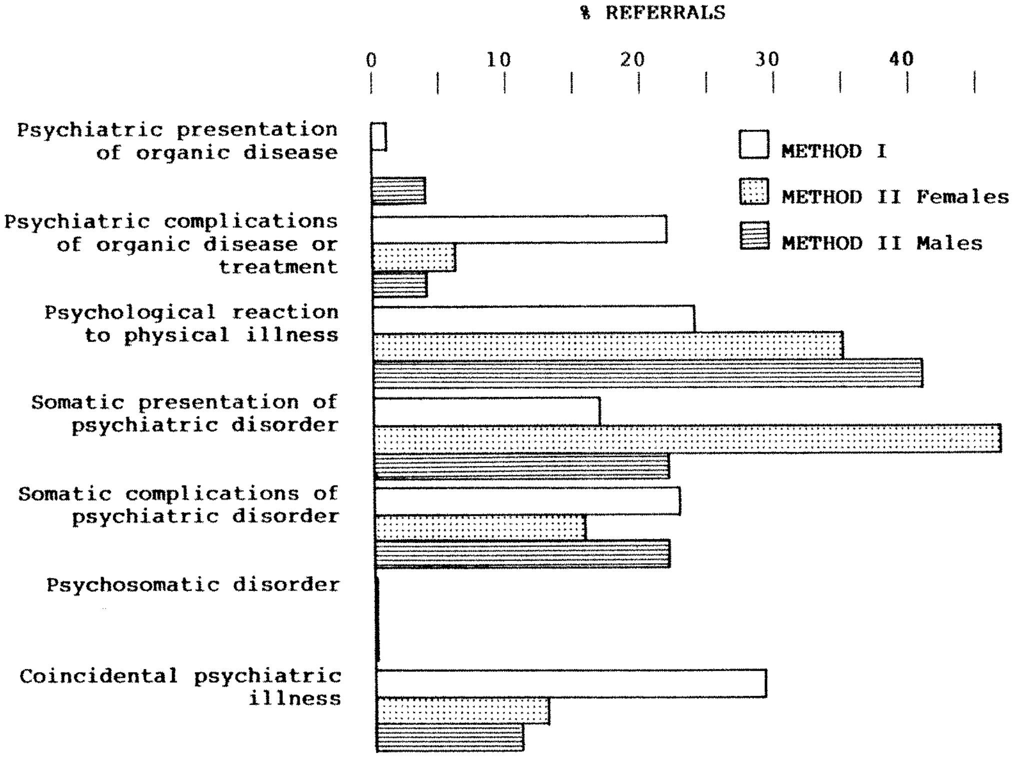

FIG. 1. The effect of two different methods of general hospital psychiatric practice on the psychiatric problems attracting referral (after Sensky *et al*, 1985). See text for further details of Methods I and II. There were significant differences between the distributions of problem types referred by the two methods (<0.005, chi-square test) and, for Method II, the types of problems for which male and female patients were referred ($P<0.05$).

method II who were *not* offered psychiatric follow-up beyond their stay on the medical ward, males tended to be seen once only for assessment, while females tended to be seen several times while they remained in-patients. This could not be accounted for by differences in the particular problems with which patients of either sex were referred. The fact that the psychiatrist was male could be relevant, but a similar pattern might then have been expected in follow-up of referrals by the other method. This did not occur. Another contributing factor could have been the fact that most of those making referrals were female.

Pathways to psychiatric care in the general hospital

The topics discussed above constitute only part of general hospital psychiatry but illustrate the complexity of the process whereby patients in that setting come to be recognised as psychiatrically ill, are referred to psychiatrists and subsequently have treatment. A similarly complex process occurs in primary care settings. Goldberg & Huxley (1980) proposed a model of psychiatric referral which views people with psychiatric disturbance passing from the community to psychiatric care through a series of settings or "levels" by means of a number of selective filters, each with its own distinctive features. The same model lends itself to general hospital settings [Fig. 2]. Elucidation of the components of this model and its features has helped to inform the psychiatrist's work in primary care, and there is every reason to believe that the same will be possible in general hospitals. No model can provide answers, but this one affords the opportunity to focus on some important questions, notably how needs are translated into demands. General hospital psychiatry emerged as a subspeciality in response to the recognition of an apparently underserved patient population (Mohl, 1983). Unfortunately, needs such as this are not necessarily expressed as demands,

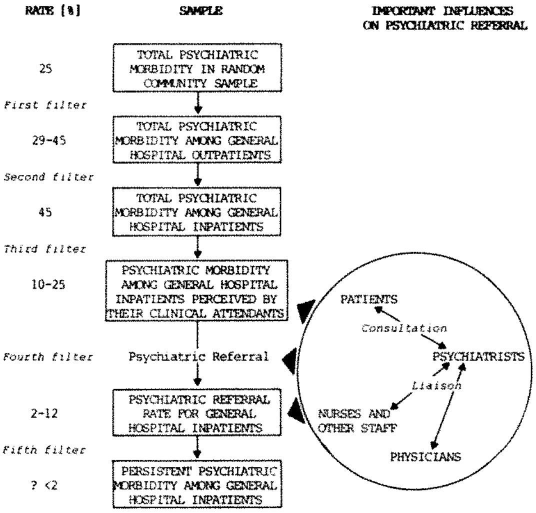
RATE [%]
SAMPLE
IMPORTANT INFLUENCES ON PSYCHIATRIC REFERRAL
25
TOTAL PSYCHIATRIC MORBIDITY IN RANDOM COMMUNITY SAMPLE
First filter
29–45
TOTAL PSYCHIATRIC MORBIDITY AMONG GENERAL HOSPITAL OUTPATIENTS
Second filter
45
TOTAL PSYCHIATRIC MORBIDITY AMONG GENERAL HOSPITAL INPATIENTS
Third filter
10–25
PSYCHIATRIC MORBIDITY AMONG GENERAL HOSPITAL INPATIENTS PERCEIVED BY THEIR CLINICAL ATTENDANTS
Fourth filter
Psychiatric Referral
2–12
PSYCHIATRIC REFERRAL RATE FOR GENERAL HOSPITAL INPATIENTS
Fifth filter
? <2
PERSISTENT PSYCHIATRIC MORBIDITY AMONG GENERAL HOSPITAL INPATIENTS
PATIENTS
Consultation
PSYCHIATRISTS
Liaison
NURSES AND OTHER STAFF
PHYSICIANS

FIG. 2. The pathway to psychiatric attention in the general hospital (modified from Sensky & Greer, 1985, after Goldberg & Huxley, 1980). Each prevalence figure relates to psychiatric morbidity or referral rates in the samples adjacent to it (below the second filter in the figure, the rates refer to percentages of total general hospital in-patients). These data are derived mostly from references cited in the text

and there may be demands for a service which are not based on an underlying need (Wing, 1972). In general hospital psychiatry, the relationship between needs and demands remains obscure and the responses of practitioners to the demands made of them vary considerably. Both these factors may serve to fuel the criticism that general hospital psychiatry lacks any coherent foundation (*British Medical Journal*, 1981). In this respect, the psychiatrist's tasks relate to his responses to the demands of patients and others while his role represents the perceived needs for his services.

The planned running down of large mental hospitals and concurrent expansion of psychiatric units attached to district general hospitals has brought psychiatrists in closer contact with their fellow clinicians and opened new possibilities for collaboration. It is important to discover how this collaboration can be most fruitful. In order to facilitate this, there is a need to characterise the different types of psychiatric morbidity shown by general hospital patients, for psychiatrists, physicians and other professionals to collaborate in learning how to recognise these and discovering more fully how they come to attract referral. Only then will general hospital psychiatrists be in a position to address one of their most important goals, namely the demonstration of the efficacy of their intervention on general medical and surgical wards.

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Tom Sensky, BSc, PhD, MB BS, MCRPsych, *Lecturer and Honorary Senior Registrar, Department of Psychiatry, Charing Cross and Westminster Medical School, Fulham Palace Road, London W6 8RF*

(*Accepted 5 June 1985*)

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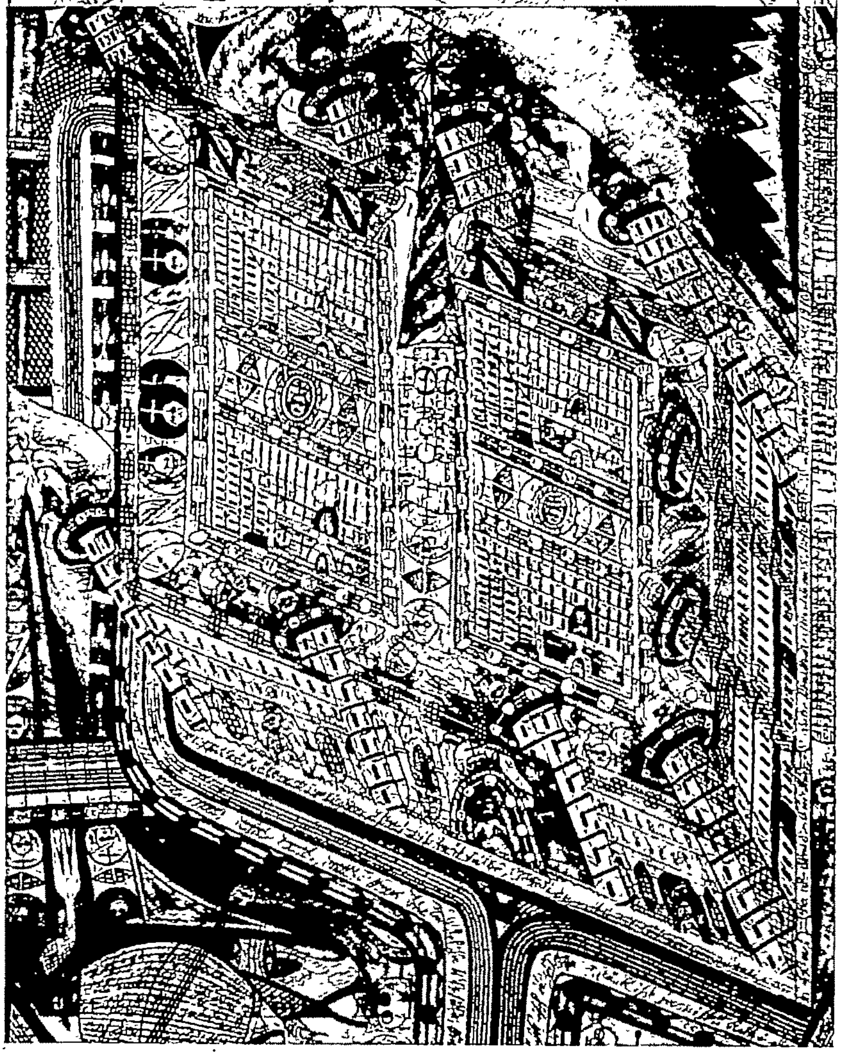

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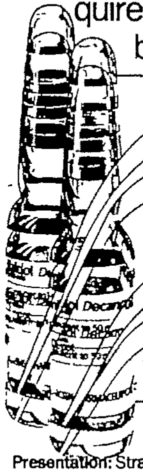

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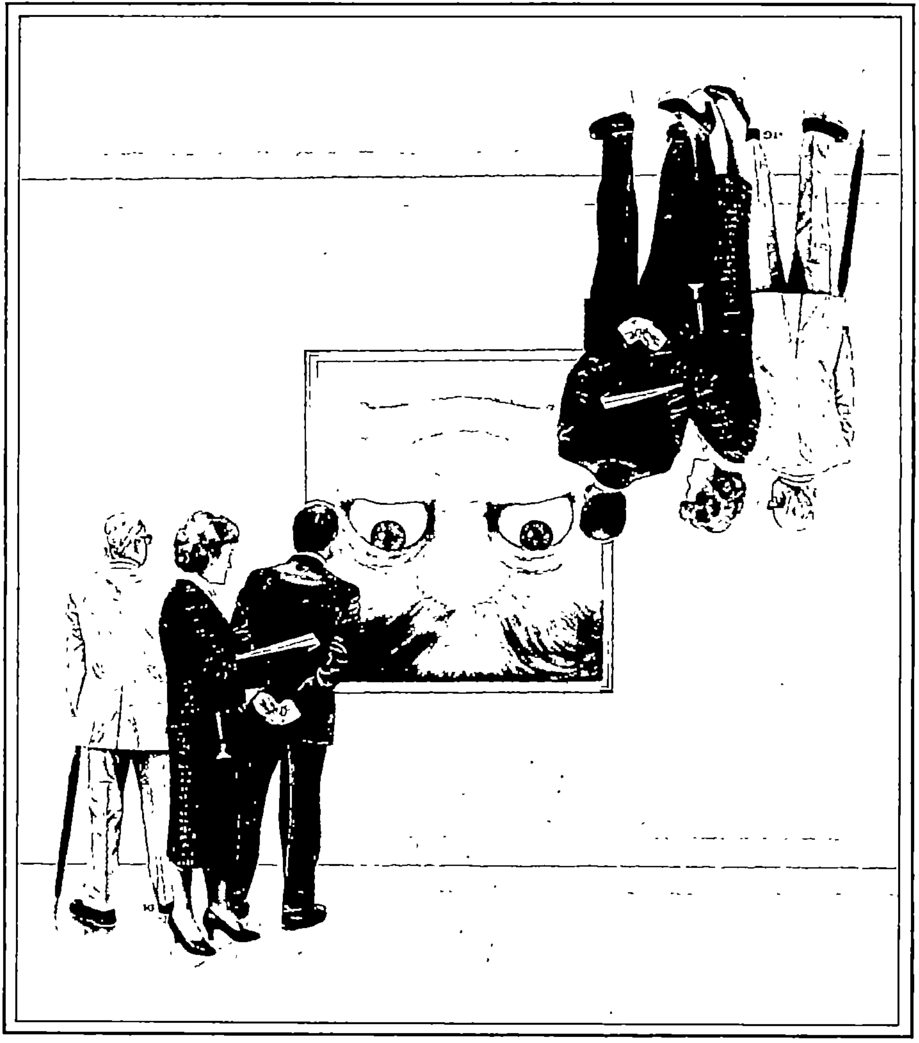

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1) Johnson DAW Br J Psychiat 1975; 126: 457-461.

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British Journal of Psychiatry (1986), **148**, 159–164

An Evaluation of a Time-limited Programme of Dynamic Group Psychotherapy

BARBARA M. DICK and KATE WOOFF

The outcome for a group of outpatients treated daily for 12 weeks in a dynamic group psychotherapy programme, was evaluated on both objective and subjective parameters. In the post-therapy year, the majority (82%) reduced their dependence on psychiatric services and showed considerable change in self-satisfaction, as assessed by an attitude test. Those available for follow-up three years later had maintained the change. There was a sub-group of patients (17%) who demonstrated an increase in service use in the post-therapy year.

The subsequent fates of patients who pass through any one branch of the psychiatric services tend to remain unknown to the staff involved, thus precluding assessment of the effectiveness of treatment. The outcome of treatment in the Wilton Unit for Psychotherapy for 49 patients, admitted between June 1976 and June 1977, has been assessed in two ways: (1) Comparison of the use of psychiatric services in the post-therapy year with that of the year preceding therapy. (2) Estimation of change in stance and attitude before and after therapy, through a questionnaire interview.

Background

The Wilton Unit for Psychotherapy opened as a Therapeutic Community, (Maxwell Jones, 1952) in February 1974 on the campus of Prestwich Hospital, a 1,000-bed psychiatric hospital, serving Salford and some adjacent areas. By 1975, as the therapeutic task emerged more clearly, a programme was instituted based on General Systems Theory (von Bertanalaffy, 1968). This included small analytical groups (Foulkes, 1975; Pines, 1983), a community meeting daily and weekly sessions using Gestalt therapy (Perls, 1969), psychodrama (Moreno, 1946), video feedback, and art therapy.

Organisation

The unit staff

The nursing staff consisted of a sister, a staff nurse, and two SEN's, a consultant psychiatrist with a special interest in psychotherapy (BMD) attended for three sessions weekly. An occupational therapist attended weekly, and a senior registrar in psychotherapy worked at the unit for the last nine months of the study. Three trainee social workers were each on placement for three months during the study period.

Selection and admission procedures

With the aim of matching patients appropriately to the therapy, the policy was to select patients with a diagnosis of neurosis, and to exclude those poorly motivated or with rigid defence systems suggestive of underlying psychosis.

The programme

A maximum of 18 patients at any one time functioned as a slow-open group and co-incidentally as three closed small analytical groups in different stages of development. An assessment period allowed for the gradual assembly of the six to eight patients comprising each small group.

Patients were required to attend five days a week for 12 weeks (60 sessions). The daily programme started with the small analytical groups, which were each conducted by the same nurse therapist throughout the therapy period. These were followed by a community meeting of all patients and staff, and family members and other workers were included when appropriate. Here, explicit rules and guidelines, which included sanctions against all physical violence and drug and alcohol abuse, promoted the ventilation of anger in relation to authority figures of the past. There followed structured group sessions which included psychodrama, art expression, encounter exercises, video feedback, volley ball, and relaxation groups.

Preparation for the ending of therapy was seen as an integral part of the therapy for both patients and therapists. The aim was to avoid the reinforcement of the experience of failure to mourn for the insecure attachment and losses of childhood, and to provide an enabling experience of parting.

Individual therapy ceased after full-time admission to the Unit, but each week BMD monitored the gradual withdrawal of medication for each patient and provided sick notes where appropriate, by agreement with the GPs. At weekly staff supervision meetings, both the operation of the small groups, and the progress of individual patients, were reviewed. Further group psychotherapy teaching was regularly sought in outside workshops, seminars, and group experiences. The unit aimed to maintain a good communication network with other hospital departments and community mental health services, and unit policy was reviewed weekly.

Evaluation methods

All Salford patients starting therapy at the unit between June 1976 and June 1977 who remained in the Salford area for at least one year after discharge were included in the study. Three patients only had moved from the Salford area before this follow-up period had expired, so that their exclusion does not unduly skew the study group. Twenty-three men and 26 women, aged between 16 and 50, were identified; one patient attended for two periods of therapy during the study period, and each episode has been included separately, bringing the sample size to 50.

For the purpose of analysis, the patients who completed at least 25% of possible attendances in each treatment episode were deemed to have received therapy, and are referred to as the treated group ($n = 40$). Those who completed less than 25% of possible attendances and were deemed not to have received therapy are referred to as the untreated group ($n = 10$). The distribution of attendances out of a possible maximum of 60 illustrates the emergence of these two distinct groups: 34 out of 40 treated patients attended over 30 times, whereas nine out of ten untreated patients attended less than ten times. There were no significant differences of age, sex, or diagnosis between the two groups, as measured by Fisher's Exact Test.

Table I illustrates the analysis of patient's symptoms and diagnoses, as recorded on the Psychiatric Register, the diagnoses were made by psychiatrists not involved at the Unit. It can be seen that the declared policy of not admitting patients with psychoses was not always applied. This was due to the economic and political climate, which put considerable pressure on staff to admit all referred patients.

Twenty-seven patients were known to have had previous psychiatric in-patient care, and the Wilton Unit was their initial treatment for only four.

TABLE I

Patients' diagnoses/symptoms recorded on Psychiatric Register. Some patients have multiple diagnoses

Diagnosis	*Treated* ($n = 40$)	*Untreated* ($n = 10$)
Psychosis	2	2
Depression	13	5
General anxiety	13	1
Phobic anxiety	3	0
Hysteria	1	0
Hypochondriasis	2	0
Obsessions and compulsions	2	0
Sex problems	3	0
Personality disorder n.o.s.*	11	2
Specified personality disorders		
Psychopathic	2	0
Depressive	1	0
Inadequate	2	0
Dependent	1	0
Vulnerable	1	0
Immature	2	0
Hysterical	0	1
Drug/alcohol problems	2	0
Situational stress	3	0
Other	1	1
TOTAL	65	12
Mean age	33	30
% Male	52	40

*not otherwise specified

Pre-and post-therapy service use

Information concerning the patients' pre- and post-therapy use of specialist psychiatric services has been analysed, using data obtained from the Salford Psychiatric Register. Since 1968, the Register has recorded details of the psychiatric services used by patients having Salford addresses, and its methods have been described elsewhere (Fryers, Freeman & Mountney, 1970; Fryers & Wooff, 1973).

Data, which are patient-based and cumulative, provide demographic, social, and diagnostic information as well as recording service use. The services covered include: admission and discharge dates from inpatient and day patient care, outpatient attendances, and referrals to and discharges from social work care. Deaths and address changes are also recorded. Diagnostic information is coded using the Camberwell Register system (Wing, 1970).

Pre-therapy service use was measured for the 365 days preceding the start of therapy and post-therapy service use for the 365 days following discharge from the unit.

The changing interface between GP and psychiatric service (Williams & Clare, 1981) and evidence of extensive involvement of the GP services in the treatment of psychiatric illness (Kessel, 1960; Shepherd *et al.*, 1966, Goldberg & Blackwell, 1970; Bransby, 1974; Goldberg & Huxley, 1980) suggest that any evaluation of the outcome of psychiatric services should take account of the primary care given. In 1980, a research worker was funded to investigate GP treatment of the 32 treated patients, who had minimal or no specialist service use after therapy.

Questionnaire

The questionnaire, based on one used in an earlier study (Dick, 1975) was piloted and amended between January 1976 and May 1976. It aimed to explore patients' attitudes in two different ways by using:

(a) Highly structured sections of the questionnaire to measure patients' satisfaction with themselves and their life situations in relation to the following eight parameters: Relationship (home and work); work performance (home and work); leisure; sex life; physical health; self-understanding; self-image; symptoms.

(b) Open-ended questions designed to record information on any change in patients' attitudes towards their illness, before and after therapy.

Patient interviews

First interview (first week of therapy)

During the first week of attendance at the unit, a questionnaire interview was carried out by one of the authors (KW), an independent research worker, otherwise unconnected with the unit. The independent status was made clear to all patients, in order to minimise the likelihood of their replies being influenced by fears of feedback to unit staff.

Second interview (final week of therapy)

Results were recorded only for those patients completing the whole of the 12-week course. An attempt made to interview those who had left the unit before the final week of therapy had a poor response, and a follow-up home visit for every patient was at that time not possible.

Third interview (three years after unit admission)

The whole sample of patients was followed-up and interviewed, again by an independent researcher, between June 1979 and June 1980, i.e. three years after starting at the unit.

The results of 'change' reported here relate to the highly structured questions. The answers to questions on each parameter were separately rated on a five-point scale, ranging from 1 (very satisfied) to 5 (very dissatisfied). The difference in satisfaction recorded at each interview was used to calculate the 'change score' for each parameter. These were summed for each patient, and the final score calculated as a ratio of 'change' to 'no change'. As one of the aims of the unit was to promote 'change' *per se*, this was viewed as a global phenomenon and all parameters were assigned equal weight.

Results

Pre-and post-therapy service use

Table II summarises the use of psychiatric services for the year before and the year after therapy. In the treated group, use of all services (days for in-patients and day patients, and appointments for out-patients) fell and the decrease in two of these three types of care was statistically significant ($P<0.02$) for in-patient days and $P<0.001$ for out-patient attendances (Wilcoxin Matched Pairs Signed Ranks Test). The untreated group was not being used as a control group, for reasons discussed later, but it is worth noting that no significant reduction in service used occurred in this group of patients.

Figure 1 illustrates service use, before and after therapy for each individual patient, and shows that 33 (82%) patients reduced their use of psychiatric services. It also shows that a sub-group of seven patients actually increased their service use over the same period; this sub-group had the same mean age (33) as the rest of the treated group and there was a higher, though not statistically significant proportion of men in it. The diagnostic composition of the two groups was dissimilar. The proportion of patients having a diagnosis of personality disorder, not otherwise specified was 21% in the decreased service use group, and 57% in the increased service use group, although the probability of this result or one more extreme, using

TABLE II

Use of psychiatric services in the pre- and post-therapy year—treated and untreated groups

	Pre-therapy year						*Post-therapy year*					
	In-patients		*Day-patients*		*Out-patients*		*In-patients*		*Day-patients*		*Out-patients*	
	No. of days	*No. of pts.*	*No. of days*	*No. of pts.*	*No. of attns.*	*No. of pts.*	*No. of days*	*No. of pts.*	*No. of days*	*No. of pts.*	*No. of attns.*	*No. of pts.*
Treated ($n=40$)	900	16	524	6	84	33	347	7	507	5	33	17
Untreated ($n=10$)	111	7	65	2	35	10	304	4	362	3	33	6

NB: Day-patient days include both attendances at Local Authority Day Centre for the mentally ill and Day Hospitals

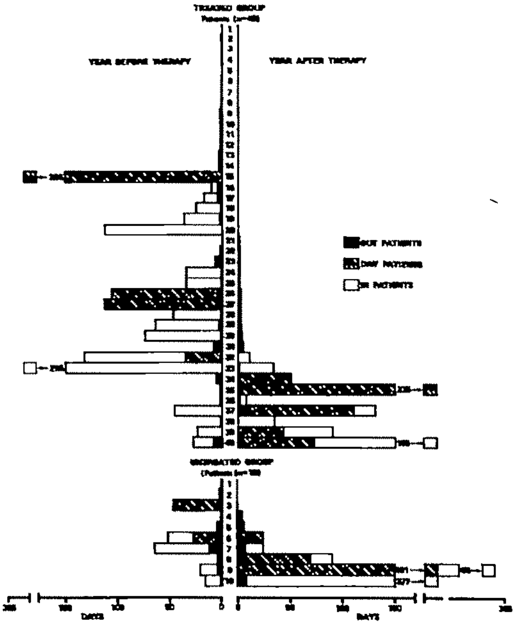

FIG. 1. Individual patient's service use one year before and one year after therapy.

Fisher's Exact Test, does not reach the 5% significance level.

A four-year follow-up of patients' service use found that of the 29 treated patients available for follow-up (ten having left the area) 23 (79%) had no contact with the psychiatric services. Six (21%) were in contact with psychiatrists.

G.P. follow-up

Of the 33 patients who had reduced their service use in their post-therapy year, the GP records of 16 were available to a research worker at four-year follow-up. Seven had attended their GPs less than twice a year, and had received no psychotropic medication. Six had received only minimum prescriptions of tranquilisers and one had been referred to a private hypnotherapist. Only two patients had been re-referred to the psychiatric service. In spite of the small size of the sample (accounted for by movement from the area and GP reluctance to allow access to notes), our findings suggest that the reduction in the use of specialist psychiatric services was not achieved at the expense of the primary care services, and the reliance on all forms of medical assistance had decreased.

Questionnaire interviews

First interview (First week of therapy)

The results of this interview were used to establish baseline data on each patient's satisfaction with his/her life style.

Second interview (Final week of therapy)

Of the 28 patients in the Treated group who were interviewed during the final week of therapy, the mean 'change score' was 70% (SD 16%).

Third interview (Three years after unit admission)

The results of the final questionnaire interviews shows a mean 'change score' of 66% over the first interview in the Treated Group (SD 18%) and 79% in the Untreated group (SD 10%). There were no significant differences on any specific parameters.

Analysis of the response rates for the final interviews, i.e. three years after starting at the Unit, showed no statistically significant differences between the Treated and Untreated Groups, in so far as movement from the area or refusal to be interviewed were concerned.

Therapists' evaluation of patients

Confirmatory evidence of change for the majority, was observable by both therapists and patients themselves during therapy, and concerned the growth of spontaneity and the ability to play and have fun. "I have never before in my life felt happy. . . . . " and "I feel I can trust some people. . . . " or "I have been back to school and this time I have learnt something" are typical of observations made by patients. Some patients were notably different from the majority, in that during therapy, they increasingly displayed behavioural patterns characterised by angry outbursts and physical violence to self and others, without signs of increase in self-understanding. The objective finding that a group of patients increased their service use in the year following therapy was confirmed by therapist observation that therapy exacerbated symptoms in some patients.

Discussion

Strupp & Bergin (1969) have emphasised the importance of the specificity of the task of therapy and of valid measures of outcome in evaluation studies of dynamic psychotherapy. The task here was to facilitate a change of stance and attitude in that symptoms become seen by their sufferers to have meaning rather than to require tranquilisation and, with the promotion of this insight, to become independent of psychiatric services.

In retrospective studies, the outcome is likely to be over-determined. In this particular one, a control group was not used, in that it required the matching of complex entities unrelated to therapy needs, and the unconditional acceptance of the therapy, which is at variance with the therapeutic alliance required for dynamic psychotherapy. Indeed, acceptance of treatment was likely to have been a significant difference between the treated and untreated groups of patients. Thus, there has been no attempt here to consider those who withdrew from treatment (the Untreated group) as a control group. It is of interest, however, that they did not demonstrate a comparable pattern of reduction in service use after Unit admission. For these patients still available for follow-up four years later, this difference still remained.

This study aimed to provide outcome measurements of the task in two ways—the one objective and the other subjective. Thus, we examined the change in patients' use of psychiatric services before and after therapy, and used their own feelings to establish the degree of personal change they experienced. The results show that the majority of Treated patients reduced their in-patient and out-patient service use significantly in their post-therapy year, and that this reduction was maintained at follow-up 4 < 5 years later.

The reduction in in-patient and out-patient service use was not a shift towards day care, for this was also reduced. Nor does the sample investigated indicate the substitution of GP for specialist services. Information from the Psychiatric Register (Wooff, 1984; British Psychiatric Registers, 1984; Wooff, Freeman & Fryers, 1983) shows a steady increase in the use of psychiatric services in Salford, and confirms that the reduction in service use observed is not just a reflection of an overall trend.

On the subjective parameter i.e. the questionnaire, consideration must be given to the part played in achieving the considerable changes in stance and attitude by the gradual reduction in psychotropic medication and by the "halo" effect fostered by the shared intimacy of therapy, but change was maintained, as the three-year follow-up shows. The Untreated patients also showed great subjective positive changes, three years after Unit admission, suggesting that both groups had become adjusted to their respective statuses, that of non-patient and that of patient. This consideration of the difference between the Treated and Untreated groups in terms of objective and subjective methods of assessment emphasises the importance of using both measures in the evaluation of psychotherapy—a field which frequently relies exclusively upon the use of subjective parameters.

The emergence of a sub-group of seven treated patients who, unlike the others, increased their service use in the post-therapy year demonstrates that dynamic group psychotherapy is not uni-directional in terms of positive change, in spite of careful selection. One of this sub-group was admitted in error with a diagnoses of manic-depressive illness, but the six others although not suffering from a psychosis, responded notably differently from majority.

The behaviour of the patients in this group conformed to the patterns described as those of borderline patients (Gurderson & Singer, 1975) or the borderline syndrome (Kernberg, 1975). The borderline syndrome or borderline personality disorder is arousing increasing interest, and is now included in the Americn Psychiatric Association Diagnostic and Statistical Manual Ill. Listed characteristics of the condition include impulsivity, self-destructive and damaging behaviours associated with interpersonal relationship difficulties, short-lived psychotic episodes, and identity confusion. Kernberg (1975) recognised this constellation of symptoms and behaviour as indicating ego weakness, with deficits in anxiety tolerance and impulse control, and the development of sublimatory channels. The treatment or borderline syndrome patients can be expected to be long and difficult, requiring as it does an experience of secure relationships, never previously encountered (Pines, 1980; Winnicott, 1954).

The diagnosis of borderline personality disorder for this sub-group has been made retrospectively, and is supported by the findings of their increased use of the psychiatric services. In psychotherapy, as in medicine, the requirement is to match treatment to patients' diagnoses, prospectively formulated. The reality, however, is that the response of the patient to the treatment is an essential part of the monitoring of the initial diagnostic assessment.

On objective and subjective parameters, the majority of patients in this study responded positively to a time-limited group psychotherapy programme. The minority group, whose response was in marked contrast to the others, responded with exacerbation of symptoms and destructive behaviour during the therapy; after it they had increased use of the psychiatric services. It is postulated that in their case, the nature of their symptoms indicated a deep-seated personality disorder rather than neurosis.

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*Barbara M. Dick, MB ChB DPM, *Formerly Consultant Psychiatrist with Special Interest in Psychotherapy, Salford Health Authority. Hope Hospital, Eccles Old Road, Salford M6 8UD.*

Kate Wooff, MSc. *Research Fellow, Department of Community Medicine, University of Manchester, Stopford Building, Oxford Road, Manchester 13.*

*Correspondence

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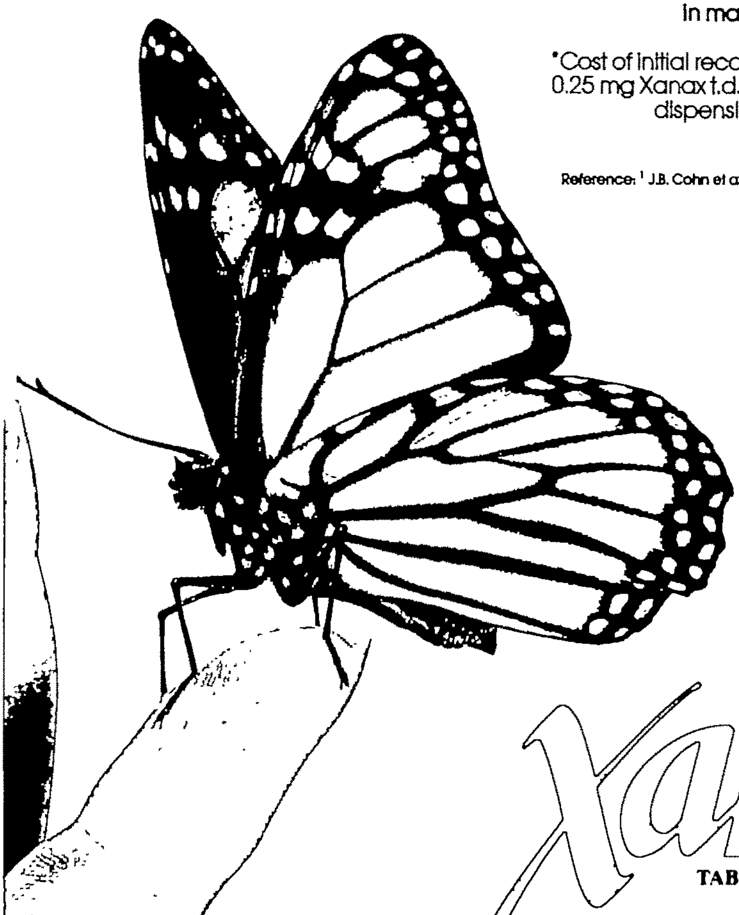

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Parental Loss by Death in the Early Childhood of Depressed Patients and of their Healthy Siblings

C. PERRIS, S. HOLMGREN, L. VON KNORRING and H. PERRIS

The incidence of parental loss by death before the age of 15 was investigated in a series of 200 depressed patients, sub-divided into unipolars, bipolars and neurotic-reactive depressives, and in their healthy siblings at risk. The age of onset of illness of patients who had lost a parent before 15 was compared with that of depressed controls. No excess of parental loss at any age was found in any of the patient sub-groups, as compared with their healthy siblings, nor did parental loss affect the age of onset of later depression. The results do not support the assumption that the loss of either parent by death in early childhood is significantly associated with depression in adult life, though parental death may be an important variable for individual patients.

Since Freud (1917) related depression in adults to reactivation of object loss experienced during childhood, and Bowlby (1969, 1980) presented his theory on attachment and loss, several attempts have been made to verify the hypothesis of a higher frequency of parental loss during the childhoods of depressed patients, as compared with controls. Reviews by Granville-Grossman (1968), Lloyd (1980), Tennant *et al*, (1980), and Crook & Eliot (1980) have shown that the results of these efforts have been inconsistent. In fact, whereas some studies showed a significantly higher incidence of parental death—e.g. Brown (1961), Forrest *et al*, (1965), and Birtchnell (1972)—others have been unable to find any such difference (Pitts *et al*, 1965). Also, when the possible impact of other variables, e.g. age of parents, social class, and place of birth is taken into account, the results remain inconsistent. Tennant *et al*, (1980) have recently advanced the alternative hypothesis that parental death during childhood may not represent a predisposing factor to depression in adulthood, but may nevertheless favour illness behaviour, thus increasing the probability that the person will seek treatment when depressed.

Pfohl *et al*, (1983) compared the records of 129 depressives, 155 schizophrenics, and 63 manics, finding that the depressives had experienced early maternal death 3.4 times as frequently as the schizophrenics, and twice as frequently as the bipolars.

Findings in previous studies by our own group have also been inconsistent on this subject. Perris (1966) investigated the occurrence of parental loss in the childhood of 145 bipolar and 150 unipolar patients, and compare the results with figures from the general population, obtained from the literature. The incidence of parental death before the age of 15 appeared to be no higher in either of the patient groups than in the general population. This agreed with the findings of a similar investigation by Angst (1966). d'Elia & Perris (1971) took into account 28 bipolars, 51 unipolars, 40 patients suffering from reactive depression, and 36 suffering from a depressive disorder that could not be classified in any of the previous groups. In this series, whereas no difference was found in relation to overall parental deaths before the age of 15, reactive patients showed a significantly higher frequency of parental death before the age of six than patients in the other groups.

In a third study (Perris & Perris, 1978), parental loss during childhood was investigated in a series comprising 175 unipolar patients, 195 bipolars, 84 non-psychotic depressives, and 70 suffering from cycloid psychosis; both the sex of the patient and two age-limits (as in the 1971 study) were taken into account. The results showed no difference among the sub-groups of depressed patients, and only the female cycloid psychotics showed an excess of parental deaths before the age of 15. However, in all four groups, parental *deprivation* before the age of 15 appeared to be consistently high.

All our previous studies compared sub-groups of patients suffering either from an affective disorder or from a disorder of still uncertain nosological classification, and it was not therefore possible to draw any conclusion as to whether our findings in depressives differed from those in a control population. Moreover, no correction was made for many of the confounding factors mentioned above.

For these reasons, a new and different study was planned, within the framework of a larger investigation of depression carried out in our Department, to compare the incidence of parental death in early childhood in a series of depressed patients and in the healthy siblings. We assumed that this procedure, not yet to our knowledge applied elsewhere, would allow us to keep under control the confounding factors identified by other authors, since the patients and controls would have shared very similar social environments during their upbringing. We also planned to take into account the exact age of the patient when parental death occurred, to minimise any risk that grouping in broader age-groups might mask the effect of very early loss.

In the 1966 study by Perris, it had been found that unipolar patients who had grown up under disturbing conditions had become ill for the first time at a significantly younger age than patients reared in an ordinary environment. The variable "disturbing conditions during childhood" in this study, however, covered not only loss of a parent by separation or death, but also such circumstances as severe conflict between the patients and/or the patient's illegitimacy, with or without the subsequent marriage of the parents. Roy (1980) investigated whether the occurrence of parental loss by separation or death before the age of 17 differed between bipolar and unipolar patients. The only statistically significant finding in this study was that death of the father before the age of 11 had occurred more frequently in the group of cases (n = 136) with an onset of illness after the age of 30. In the present study, we aimed to investigate again whether parental loss in childhood showed any relationship to age at onset of illness.

Method

Patients suffering from a primary depressive disorder and consecutively admitted to the Department of Psychiatry at the Umeå University between 1977 and 1980 participated in a comprehensive study of depression in its various biological, psychological, and social aspects. Among the variables taken into account was an ascertainment of parental loss by death in early childhood.

From a diagnostic point of view, the patients were divided into unipolars (n = 60), bipolars (n = 73), and those suffering from a reactive-neurotic depression (n = 67) according to diagnostic criteria presented in detail elsewhere (Perris, 1966, 1975; d'Elia, von Knorring & Perris, 1974). The diagnostic classification into sub-groups was made from the records by two experienced psychiatrists. In the few instances where disagreement occurred, the case was discussed jointly; if no decision could be reached then, the patient was assigned to a holding group ("non-classified depressive disorder") and was not included in the present series.

All the subjects had also participated in a family study aimed at assessing morbidity among their first-degree relatives, Part of which has been published (Perris *et al*, 1982, 1985). For the purpose of that study, information about parents and siblings was obtained from parish registers. Such information also included the date of death of any first-degree relative. Morbidity among first-degree relatives was calculated using a combined family history study approach. Correction for the population at risk was made by using Weinberg's abridged method (Weinberg, 1925). In the family study, the siblings affected by an affective disorder had been identified, so that it was possible to separate affected from non-affected siblings within each family.

TABLE I

Patients and siblings who lost either parent before the age of 15. Sex and age at loss. Unipolar group (n = 60)

	M: male Loss of father			*F: female Loss of mother*		
Age (yrs)	*Patients*	*Healthy siblings*	*Ill siblings*	*Patients*	*Healthy siblings*	*Ill siblings*
1	M					
2		M			F	
3		FF				
4	F			(F)*	F	
5		M			F	
6		M				
7		F		F	MF	
8		F			F	
9			M		MF	
10	F			M	M	
11			M		M	
12		M			MM	
13	F	F		F	MF	F
14		MMF		F		
15				F	MF	

*(only child)

Age at first onset of illness was ascertained during direct interviews with the patients and with at least one of the closest relatives.

For the present comparison, the occurrence of parental death for each year of age up to 15 was calculated separately for the patients, for their affected siblings, and for their healthy siblings divided by sex. Only the corrected number of siblings at risk was taken into account for the comparison. We assumed that by applying the calculation of parental death the same age correction currently used when assessing morbidity risks, we would reduce error due to the fact that not all healthy siblings had yet passed the whole risk period.

Results

The results referring to the loss of either parent in the three patient groups and for each year of age are presented in Tables I to III, and an overview of the proportion of all

TABLE II

Patients and siblings who lost either parent before the age of 15. Sex and age at loss. Bipolar (n = 73).

	M: male Loss of father			*F: female Loss of mother*		
Age (yrs)	*Patients*	*Healthy siblings*	*Ill siblings*	*Patients*	*Healthy siblings*	*Ill siblings*
1		M			MMF	
2					M	
3		F		F	F	
4		F		F		
5	F					
6						F
7		FF	MF			M
8		MFF				
9	F		F	M		
10		MMMMF	F		F	
11		FF			F	
12		F		F	F	F
13	MMF	M	M		MFF	
14	M	MMM			M	
15	M	MM	M		MF	F

TABLE III

Patients and siblings who lost either parent before the age of 15. Sex and age at loss. Neurotic—reactive group (n = 67)

	M: male Loss of father			*F: female Loss of mother*		
Age (yrs)	*Patients*	*Healthy siblings*	*Ill siblings*	*Patients*	*Healthy siblings*	*Ill siblings*
1	F					
2		M				
3		F		M		
4	F	M			F	
5		F				M
6	F	MM			M	
7					MM	
8		M			MF	
9	M	MF			MFF	
10		MF		F		F
11		M			F	
12			F		M	
13		MF		M	F	
14	(F)*	M		M	MF	M
15					M	

*(only child)

TABLE IV

Loss of either parent before the age of 15 in patients and in their ill siblings and healthy siblings

	Loss of father						*Loss of mother*				
Diagnostic group n and Sex	*Siblings at risk n†*	*Healthy siblings n*	*% loss*	*Ill siblings n'*	*% with loss of father*	*Patient's proportional loss*	*Healthy siblings n*	*% loss*	*Ill siblings n*	*% with loss of mother*	*Patients' proportional loss*
Unipolar											
(23 Male	51.1	6	11.6	2	3.9	1/23	9	17.5	—	—	1/23
(37) Female	96.5	6	6.2	—		3/37	9	9.3	1	1.0	5/37
Bipolar											
(33) Male	70	12	17.1	3	4.3	4/33	7	10.0	1	1.4	1/33
(40) Female	100	10	10.0	3	3.0	3/40	8	8.0	3	3.0	3/4
Neurotic-Reactive											
(23) Male	39.5	10	25.3	—	—	1/23	8	20.3	2	5.1	3/23
(44) Female	82	5	6.1	1	1.2	4/44	7	8.8	1	1.2	1/44

†No. of siblings at risk refers to age-corrected figure, obtained by the method currently used in family studies is therefore not necessarily a whole number.

subjects with parental death before 15 years of age in Table IV. The proportion of parental deaths is consistently higher among the healthy than among the ill subjects, independently of the sex and age of the subjects when parental death occurred and of the sex of the dead parent.

The age at onset of illness for patients with and without parental loss before the age of 15 did not differ in any part of the diagnostic sub-groups.

Discussion

Several investigations, including some by our group, have been aimed at verifying the hypothesis of a higher incidence of early parental death in depressives than in other patients and healthy controls, but the results obtained have been inconsistent. Some of these earlier studies have been criticised for not having taken into account the possible confounding effect of decade of birth, parental age, sex of the lost parent in relation to the sex of the patient, and social class.

To avoid most of these sources of error, the incidence of parental death in early childhood in the present series of depressed patients was compared with that in their healthy siblings at risk. The patients were divided into bipolars, unipolars, and neurotic-reactive depressives, according to given definitions. In none of the sub-groups was an excess of parental death found at any age before 15. Since our procedure allowed for control of all confounding variables not consistently taken into account in earlier studies, it must be concluded that parental loss by death before the age of 15 is not associated with depression in adults. Also, no difference in age at onset of illness was found between patients who had lost a parent before 15 years of age and those who had not. The present series is admittedly small, and thus the results should be treated cautiously, but our findings clearly support those obtained by other authors in larger series (e.g. Birtchnell, 1972).

The search for a possible association between parental loss in early childhood and depression in adult life has been stimulated by the writings of Freud and Bowlby. However, it now appears likely that parental loss by death is not the crucial variable, and that other factors should be taken into account, e.g adverse life events, which may affect sibs of different age differently, or other losses which might be more difficult to detect retrospectively. In this last respect, the lack of a warm relationship with the parents may well be much more important (Jacobson *et al*, 1975; Parker, 1983). A further study, examining this last question is in preparation.

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*Carlo Perris, MD. *Professor of Psychiatry; Chairman, Department of Psychiatry III & Director, WHO Collaborating Centre for Research and Training in Psychiatry, Umeå University Hospital, S-901 85 Umeå, Sweden.*

Sonja Holmgren, *Registered Nurse (Research).*

Lars von Knorring, MD. *Associate Professor of Psychiatry.*

Hjördis Perris, Dr med sc. *Associate Professor of Medical Psychology.*

*Correspondence

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Perceived Depriving Parental Rearing and Depression

C. PERRIS, W. A. ARRINDELL, H. PERRIS, M. EISEMANN, J. VAN DER ENDE and L. VON KNORRING

Four groups of depressed patients 47 unipolars, 21 bipolars, 34 with neurotic-reactive depression, and 39 with unspecified depressive disorder completed, after recovery, the EMBU, a Swedish instrument aimed at assessing the experience of parental rearing practices. The results for three factors: "rejection", "emotional warmth" and "over-protection" and the global judgement scores of "severity" and "consistency" in rearing attitudes were compared with those obtained from 205 healthy individuals. Depressed patients, particularly in the unipolar unspecified groups rated both parents lower than the controls on emotional warmth. Patients tended also to rate their parents as less consistent in their rearing attitudes. The variables emotional warmth and overprotection allowed 64% of the patients and 72 of the unipolar depressives to be classified correctly. These results, like those of previous studies, support the hypothesis that deprivation of love during childhood represents an important psychological risk factor in the background of depressive disorders.

Until quite recently, attempts aimed at verifying the assumption based on the theories of Freud (1917) and of Bowlby (1969, 1980) that depression in adults could be due to a reactivation of a feeling of loss experienced in early childhood have mostly been focused on quantitative aspects of parental deprivation during the childhood of depressed patients. Most studies have assessed the incidence of parental loss up to the age of 15 in depressed patients, compared with other kinds of psychiatric patients, with healthy controls, or with data from the general population. However, the results of these studies have been inconsistent, and whereas some reviewers of the literature maintain that an association between parental loss in childhood and depression in adult life seems to occur (Lloyd, 1980, others (Granville-Grossman, 1968; Tennant *et al*, 1980; Crook & Eliot, 1980) are much more critical, maintaining that this has not yet been demonstrated. Part of the inconsistency among results obtained by different authors might be due to the neglect of important confounding variables e.g. the decade of birth of the patients, parental age, the age of the patient when the loss occurred, social class, etc. A recent study of our own (Perris *et al*, 1984) which overcame most of the sources of error identified by other research workers, investigated the occurrence of parental loss in a large series of depressed patients, and compared the results with those for the patients' siblings, both healthy and ill. No excess of parental loss was found at any age in the patients group, compared with the healthy siblings, nor was there any trend suggesting a higher incidence of parental loss in the patients, when the sex of the patient and the sex of the lost parent were taken into account.

More recently, some authors have suggested that qualitative aspects of childhood deprivation should be taken into account, e.g. the patients' perception of parental rearing practices (Gay & Tonge, 1967; Raskin *et al*, 1971; Jacobson *et al*, 1975; Blatt *et al*, 1979; Parker, 1979, 1983; Perris *et al*, 1980). There are, in fact, several reasons why such an approach might be more relevant than just a quantitative study of parental loss. However, it is very difficult to ascertain retrospectively the degree of bonding between the patient and the lost parent, and to get adequate information about the possible vicarious role of other close relatives when the loss of a parent occurred. Some studies have reported that neurotic depressives had more parental loss by separation than by death (Brown *et al*, 1977; Roy, 1978), while others have recorded the frequent occurrence of severe conflicts in the families of depressed patients (Perris, 1966; Perris & Perris, 1978). In such cases, it is difficult to decide whether the climate of conflict within the family or the separation from a parent was the more traumatic. Support for the qualitative hypothesis can be found in more modern psychoanalytical views of depression Bibring (1953), for example, maintained that a predisposition to depression is due to insufficient parental love during childhood, which would fixate the child to feelings of helplessness, and Bowlby stressed that the role of the caregiver that should be empathetic and stimulating.

Raskin *et al*, (1971) and Jacobson *et al*, (1975), in studies of depressed patients, did not find any association of adult depression with overt parental loss in childhood, but evidence of an association with depriving childrearing practices; depressed patients rated their parents more negatively than normals, especially in respect of acceptance vs rejection. The results by Raskin *et al*, were confirmed by Parker, who found in a series of investigations that depression was strongly associated with patients' reports of either lower quality parental care or overprotection. Both Jacobson *et al*, and Parker also found that depriving childbearing practices were related to the severity of adult depression. To be able to examine the issues of a possible qualitative depriving childhood environment in depressed patients, we developed an instrument—the EMBU (Egna Minnen av Barndomsuppfostran)—covering areas of childbearing practices which were thought likely to be relevant for mapping parental attitudes (Perris *et al*, 1980; Jacobsson *et al*, 1980). This instrument, now available in several languages, has been successfully applied by other research workers (Ross *et al*, 1982, 1983; Clayer *et al*, 1984; Arrindell *et al*, 1983a b) and is currently used in an ongoing cross-national study of child-rearing practices and depression.

The EMBU has been applied, together with a personality inventory, to a large series of depressed patients (Perris *et al*, 1983), and results suggested that the experience of parental rearing might be relevant in shaping the particular personality structure that characterises the depression-prone individual (Perris *et al*, 1984). The present study used the EMBU in a series of depressed patients and in healthy controls. It had been hypothesised that depressed patients would report more negative and depriving rearing practices from their parents than would healthy controls.

Method

A. The series

Depressed patients of any kind, consecutively admitted to the Department of Psychiatry of Umeå University, completed the EMBU as part of a larger study of depression. The series was classified by two independent psychiatrists into diagnostic sub-groups; when there was disagreement between them, the case was jointly discussed until agreement was reached. If the patient could not be classified in any of the main groups, he/she was assigned to the "unspecified depressive disorders".

The diagnostic groups taken into account were: bipolar, unipolar, and neurotic-reactive depression, according to the definitions given in Perris (1966, 1975) and d'Elia *et al*, (1974). The characteristics of these patients were as follows:

(a) Bipolar depression: patients who had previously suffered from at least one episode of depression and one of mania and who were currently depressed when they entered the study.

(b) Unipolar depression: patients who had suffered from recurrent episodes of depression (generally at least three), mostly of a psychotic severity with a symptom-free interval between the episodes.

(c) Neurotic-reactive depression: patients characterised by a vulnerable personality structure and a proneness to depressive reactions to adverse external events, mostly of non-psychotic severity.

(d) Unspecified depressive disorder: patients who suffered from a depressive disorder, either psychotic or non-psychotic but did not fulfill the criteria for inclusion in any of the aforementioned groups, an/or on whom diagnostic agreement could not be reached.

On hundred and forty-one patients of the two sexes entered the study; this number is not the same as that in our study of parental loss by death in the early childhood of depressed patients (Perris *et al*, 1984) for two reasons. Firstly, because the other series comprises only those patients for whom complete information about parental death and age of the probands and their sibs at the time of the parental loss could be obtained from the Parish registers in the course of a family study. Secondly, because the present study of perceived parental rearing practices includes only those patients who had recovered from the depressive episode to such a degree that the possibility of depressive mood influencing the results could be excluded. The composition of the series in terms of age, sex, and diagnostic distribution is shown in tables I and II. A series of 205 healthy individuals collected previously (Perris *et al*,

TABLE I
The series: age and sex distribution

	21–30	*31–40*	*41–50*	*51–60*	*61–*	*Total*
Male	10	8	7	21	7	53
Female	10	28	15	22	13	88
Total	20	36	22	43	20	141

Chi^2 = 7.62 (df 4) *P* NS

TABLE II
The series: distribution according to sex and diagnostic group

	Unipolar	*Bipolar*	*Neurotic-reactive*	*Unspecified*
Male	18	7	16	12
Female	29	14	23	22
Total	47	21	39	34

Chi^2 = 0.44 (df 3) *P* NS

1980) has been used as controls; it consists of a sample who participated in a large cross-national study of perceived rearing practice (Arrindell *et al*, 1985)—118 males and 87 females (mean age 21.9 SD 11.5). Male subjects were unselected conscripts from the whole country; female subjects were recruited from personnel at the Hospital, the School of Nursing, and friends and acquaintances of these people.

B. Assessment of parental rearing practices

Memories of the perceived rearing practices of the parents were assessed by means of the EMBU, which is an 81-item questionnaire, answered by the subject on a four-point scale, separately for the mother and for the father. These items are grouped in 14 arbitrary sub-scales, covering the following kinds of rearing practices; abusive, depriving, punitive, shaming, rejecting, overprotective, overinvolved, tolerant affectionate, performance oriented, guilt-engendering, stimulating, favouring siblings, and favouring subject, Two additional questions refer to a global judgement about the severity of the parental rearing practices and the extent to which rearing practices have been consistent.

The EMBU was introduced to each patient by one of the members of the research team who had already had the opportunity of establishing a therapeutic relationship in the course of previous interviews, and they were asked to complete the form by themselves, but could ask for supplementary information and explanation whenever required.

Every patient completed the EMBU after recovery from the depressive episode or, at least when improvement was such that discharge from hospital was expected. None of the patients was still depressed at the time of the investigation, however, a few among them about (20%) had minor residual symptoms, mostly anxiety and sleep disturbance.

C. Statistical analysis

The statistical analysis was carried out at the Computer Centre of Umeå University (UMDAC) using standard programmes (Statistical Package for the Social Sciences: SPSS). For the present study, it was decided to use the four-factor solution suggested by Arrindell *et al*, (1983a). In their results, the following four factors emerged: rejection, emotional warmth, overprotection and favouring subject. However, only the first three of these have proved to have a satisfactory internal consistency (Cronbach alpha ranging from 0.87 to 0.91 for "mothers" and from 0.87 to 0.93 for "fathers") and to be transferable across samples (further details about the psychometric evaluation of the EMBU in multinational samples, and about its invariance across distinct populations, including the present ones will be found in Arrindell *et al*, (1985). Thus, only the first three factors have been used in the present study. The comparison between depressed probands and controls was made by means of the Kruskall-Wallis analysis of variance, followed by pairwise comparisons by means of the Mann-Whitney U test (Siegel, 1956).

Possible correlations with age were investigated by means of the Spearman rank r. A discriminant analysis between patients and controls, and between the unipolar group of patients and the controls was also carried out.

Results

Only one weak but statistically significant negative correlation with age (r—0.21) emerged. It refers to the factor "rejection" (mothers). The results of the comparison of the three factors among the different groups are presented in tables III and IV. Patients in all diagnostic groups scored lower than the controls on "emotional warmth", and this applies to both parents. However, the difference is statistically significant only for the unipolar group and for the group of "unpsecified" patients. Patients scored also lower than controls on the factor "material overprotection", but once again the difference is statistically significant only for the unipolar group, who also rated their parents as less rejecting than did the other groups.

Table V shows the results concerning the consistency of parental rearing practices and a global judgement of their severity. Unipolar patients scored their factors as more consistent in their rearing attitudes than did patients with an unspecified or neurotic-reactive depressive disorder, whereas these last groups tended ($P<0.09$) to rate their fathers as less severe in their rearing practices than did the other groups.

The results of the discriminant analysis showed

TABLE III

Mean scores and SD on the three factors in the different sub-groups. A Fathers

(N)	*Rejection*		*Emotional warmth*		*Overprotection*	
1. Unipolar (47)	33.7	8.5	44.1	10.4	28.9	5.7
2. Bipolar (21)	34.1	10.1	46.3	15.4	29.4	6.0
3. Neurotic-reactive (34)	36.7	11.3	48.2	12.4	30.9	7.9
4. Unspecified (39)	37.1	11.2	45.6	9.2	31.7	8.1
5. Healthy controls (180)	35.6	8.4	49.2	9.8	31.0	7.1
Mann-Whitney pairwise comparisons	1 vs 5 $P<0.04$		1 vs 5 $P<0.003$ 4 vs 5 $P<0.04$			

TABLE IV
Mean scores and SD on the three factors in the different sub-groups. B. Mothers

Group	*Rejection*		*Emotional warmth*		*Over-protection*	
1. Unipolar	34.7	9.8	44.2	11.1	31.5	6.4
2. Bipolar	35.3	9.5	49.5	13.2	32.2	7.0
3. Neurotic-reactive	37.5	11.4	48.4	12.3	32.7	7.0
4. Unspecified	35.0	6.3	48.5	9.3	33.4	7.6
5. Healthy controls	36.1	9.0	52.2	8.7	34.8	7.8
Mann-Whitney pairwise comparisons	1 vs 5 $P<0.03$		1 vs 5 $P<0.000$		1 vs 5 $P<0.009$	
			4 vs 5 $P<0.02$			

TABLE V
Mean scores and SD on the variables "severity of rearing practices" and "consistency in rearing attitude" in the different sub-groups and for both parents

Group	*Fathers*				*Mothers*			
	Severity		*Consistency*		*Severity*		*Consistency*	
1. Unipolar	2.8	0.79	2.1	0.69	2.8	0.70	2.1	0.54
2. Bipolar	2.7	0.78	1.8	0.79	2.8	0.77	2.1	0.77
3. Neurotic-reactive	2.6	0.92	1.6	0.89	2.9	0.77	2.0	0.90
4. Unspecified	2.3	1.13	1.6	0.89	2.8	0.71	1.9	0.82
5. Healthy controls	2.7	0.82	2.0	0.73	2.9	0.71	2.2	0.67
(Kruskal-Wallis)	<0.09		<0.002		<0.97		<0.37	
Mann-Whitney pairwise comparisons	1 vs 4	$P<0.05$	1 vs 4	$P<0.001$				
			1 vs 3	$P<0.004$				
			3 vs 5	$P<0.004$				
			3 vs 5	$P<0.01$				

standardised canonical coefficients of 0.80 and 0.32 for "emotional warmth" and "overprotection" respectively for the fathers (Wilks 0.95, $P<0.001$) with 64 per cent of cases correctly classified. For the mothers the coefficients regarding the same two factors were 0.83 and 0.28 respectively (Wilks 0.91, $P<0.0001$) with 76 per cent of the cases correctly classified.

Discussion

Our results support the assumption that the love-depriving upbringing might be an important psychological variable in the background of depressive disorders. In this respect our findings cross-validate those obtained by Parker (1983), who used a similar instrument (the Parental Bonding Instrument PBI) and who recently stressed the importance of "affectionless control" as a risk factor for depression. However, our patients did not rate their parents as more overprotective than the controls did and in fact showed opposite results, especially in the case of the unipolar patients. It is uncertain, though, to what extent the measures of "overprotection" in the PBI and in the EMBU correspond to each other. A possible reason for the difference between our results in the unipolar patients and those of Parker might be that most of our (older) unipolar patients were from rural families, in which "overprotection" might be less common.

Parker (1979) stated that patients classified as neurotic-reactive reported more negative experiences in the upbringing than bipolar patients. We did not find significant differences among these two groups, but neurotic-reactive patients rated both their parents as more rejecting than did all the other groups. In addition, neurotic-reactive patients rated their fathers as globally less severe and less consistent in their rearing practices that both unipolar and bipolar patients, and their mothers as more severe and less consistent than the other two groups. However, the number of patients in our bipolar and neurotic-reactive series is small, and it is possible that larger series would have yielded statistically significant results. The results of the discriminant analysis should be interpreted cautiously, but our preliminary findings suggest that the variables "emotional warmth", and "overprotection" (corresponding broadly to Parker's concept of "affectionless control") might discriminate depressed patients, and in particular unipolars from controls.

Unipolar patients rated their parents as less "rejecting" than did the controls, but the unipolar patients were older and a weak negative correlation between at least maternal rejection and age has been found. Thus, this difference between unipolar patients and controls might be explained, at least in part by the difference in age.

When investigating in adults memories of parental rearing practices in their childhood, the question obviously arises to what extent these memories reflect a distorted view of the parental attitudes and not actual rearing practices. Furthermore, the experience of depression might contribute to such a distorted recollection. Parker (1981) has considered these questions in the case of the PBI, where scores obtained by independent observers correlated significantly with scores obtained from subjects, thus supporting its validity. However, no independent evaluation of our patients' parental rearing attitudes could be made; this would only be possible prospectively and only when much younger patients were concerned. However, it has been argued that what is relevant is not how rearing practices have really been, but how they were perceived by the subject experiencing them (Ausubel *et al*, 1954; Ausubel, 1958). Wolkind & Coleman (1983) have pointed out the risk of a confounding effect of depression on the recall of the type of parental relationship during childhood, but their results are at variance with those of Parker (1981), who did not find any influence or depression on a selfreport measure of parental characteristics. Confounding effects have always to be taken into account in retrospective investigations of depressed patients, and in this context there is an alternative hypothesis which is well-known in the psychoanalytical literature (e.g. Arieti & Bemporad, 1978; Wolfenstein, 1966; Miller, 1981). This is that in recovered depressed patients, when defence mechanisms are restored (mainly denial and repression), there is a tendency to idealise rather than to blame their parents.

In our series, all the patients were investigated when they had recovered from their depressive mood, by staff who had had an opportunity of establishing a good therapeutic relationship with them during the illness, so that the risk of distortion should be less than in some other studies. In addition, only small size differences emerged among subgroups of patients who had suffered illnesses of different severity. Even if our results have to be interpreted cautiously, a consistent pattern is certainly emerging in the literature.

Thus, the results concerning a qualitative deprivation experienced by depressed patients during their childhood seem to be very consistent across several studies, comprising patients belonging to different diagnostic sub-groups, and independently of the instrument used for assessment. They suggest that rearing practices which deprived the child of love might be an important risk factor predisposing to depression. Studies of relationships between rearing practices and personality characteristics also suggest that the personality structure shaped by negative rearing experiences might be an important mediating link in the occurrence of depression, since both variables (Perris 1983, 1984) seem to enhance individual vulnerability to stressful life events.

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*Carlo Perris, MD, *Professor of Psychiatry & Chairman, Director, WHO Collaborating Centre for Research & Training in Mental Health, Umeå University, Department of Psychiatry, S-901 85 Umeå, Sweden.*

W. A. Arrindell, *Clinical Psychologist, Department of Clinical Psychology, Academic Hospital of the State University of Groningen, Oostersingel 59, 9713 EZ Groningen, The Netherlands.*

Hjördis Perris, Dr med Sci, *Associate Professor of Medical Psychology, Umeå University, Department of Psychiatry.*

Martin Eisemann, *Research Psychologist, Umeå University, Department of Psychiatry.*

J. van der Ende, *Research Assistant, Department of Clinical Psychology, Academic Hospital of the State University of Groningen.*

Lars von Knorring, MD, *Associate professor of Psychiatry, MRC Research Fellow Umeå University, Department of Psychiatry, S-901 85 Umeå, Sweden.*

*Correspondence

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Affective Disorder amongst Women in the General Population: A Longitudinal Study

P. G. SURTEES, S. P. SASHIDHARAN and C. DEAN

This paper reports upon a longitudinal general population survey of psychiatric disorder among a sample of women in Edinburgh. The course and outcome of the identified disorders, defined according to the RDC, are described. In addition the report documents the consequence, for the description of episodes, of adopting a diagnostic scheme which embodies hierarchical and inter-episode interval rules. Estimates of disease rates per year revealed a period prevalence of RDC disorder of 25.2% (17.6% depressive and 7.6% anxiety disorder) and an RDC new episode inception rate of 12.6%. In spite of the evident non-trivial nature of these conditions, and of the extent to which they were found to endure, contact with the psychiatric services was found to be minimal.

Our knowledge of the epidemiology of psychiatric disorders in the general population has been considerably advanced by the recent development of reliable and valid methods of case identification and definition. As a result, we now have comparable estimates of the prevalence of psychiatric disorders in particular groups and communities, which provides an empirical basis for policy decisions concerning both the allocation of resources and the development of treatment option (Boyd & Weissman, 1981). Following upon these improved diagnostic methods has been the increased consistency with which risk or vulnerability factors have been identified in association with psychiatric conditions, thereby providing clues about their genesis and suggesting areas worthy of further exploration (Hirschfeld & Cross, 1982).

To build upon the gains already made in this research, new questions should be posed concerning the evolution and the outcome of disorders identified outside treatment settings and the refinement of aetiological hypotheses. However, the extent to which these objectives can be achieved through employing cross-sectional retrospective designs is limited. To detect patterns of covariance between pathological outcome and antecedent conditions, to confirm notions about disease aetiology, to calculate disease inception rates, and to develop methods for identifying population groups at risk, prospective longitudinal designs are suggested (Mednick *et al*, 1981).

There is general agreement amongst recent studies that psychological disorders, defined as persistent dysphoric symptoms or as meeting the criteria of diagnosable "clinical" conditions, are common in the community. One month prevalence estimates of psychiatric morbidity are usually found to range from 8% to 15%. Affective disorders (almost exclusively depression) are the commonest with a one month prevalence of 6% to 9% amongst women (Dean *et al*, 1983). Estimates of the life-time prevalence of depressive disorders amongst women are rare; recent studies indicate a range from 4.9% to 8.7% for definite major depressive episodes (DSM–III criteria) but up to 25.8% for Research Diagnostic Criteria (RDC) major depression (Weissman & Myers, 1978; Robins *et al*, 1984).

Evidence suggests that episodes of psychiatric disorder which can be identified in the community are neither trivial in nature nor transient in duration, but that they incorporate symptoms frequently lasting for several months (Brown & Harris, 1982). Although much effort has gone into defining and categorising these conditions, little is known about their constituent symptoms or their outcome. There is evidence, however, to suggest that psycho-social adversity is implicated in the genesis and maintenance of some of these disorders (e.g. Brown & Harris, 1978; Surtees & Rennie, 1983). More information is available about similar disorders as detected in primary care and in hospital settings (Cooper *et al*, 1969; Paykel *et al*, 1970; Paykel, 1978; Ceroni *et al*, 1984).

A longitudinal general population survey of women in Edinburgh attempted to examine some of these issues. This paper deals with aspects of our investigation which were concerned with:

(a) assessing the outcome of psychiatric disorders identified using the RDC (Spitzer *et al*, 1978),

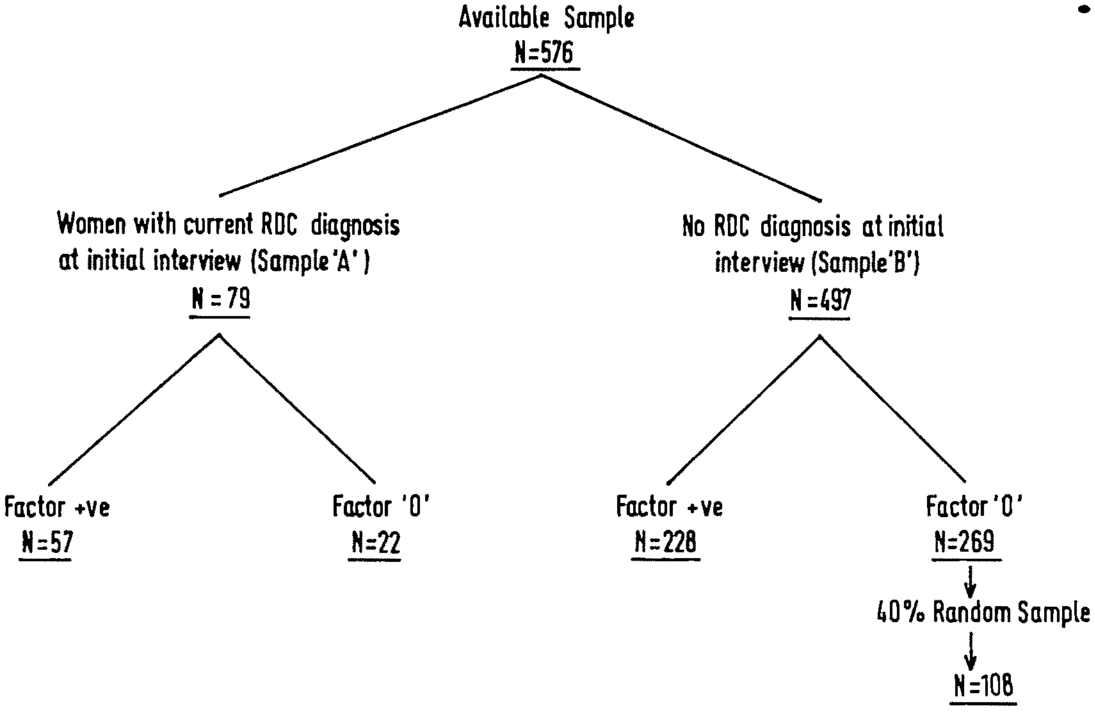
Available Sample
N=576
Women with current RDC diagnosis at initial interview (Sample 'A')
N = 79
No RDC diagnosis at initial interview (Sample 'B')
N = 497
Factor +ve
N=57
Factor '0'
N=22
Factor +ve
N=228
Factor '0'
N=269
40% Random Sample
N=108

FIG. 1. Constitution of the follow-up sample.

(b) describing the clinical nature of such disorders, and

(c) estimating disease rates and contact with health services during the period of observation.

Method

The community study was undertaken in a geographically discrete area of Edinburgh, and was restricted to a random sample of women aged 18–65 years. The initial survey obtained interviews from 576 women, representing an approximate 1 in 100 sample of those eligible for inclusion. The design had three stages: the first was cross-sectional, while a sub-sample of those women initially interviewed were approached for re-interview, six months and one year later. Details of the design and methodology of the initial survey are provided in an earlier report (Surtees *et al*, 1983). Women were selected for follow-up if they: (i) met *either* the RDC *or* the diagnostic scheme allied to the Present State Examination (PSE) (Wing *et al*, 1974; Wing & Sturt, 1978) for a current psychiatric disorder. These women formed Sample 'A'. (ii) were currently free of psychiatric disorder but had one or more of a set of putative vulnerability factors being recorded as present OR were included in a 40% random sample of those women who were both currently well and had none of the factors recorded as present. These women formed Sample 'B'.

By this strategy, we had planned to assess all those women who developed psychiatric disorder at any time during the study and to estimate the incidence of psychiatric disorder in the sub-group of Sample 'B' distinguished by the presence (Factor-positive) or absence (Factor-zero) of "risk factors". The set of ten factors chosen were: (i) none or very poor relationship with a confidant, (ii) none or very little diffuse support, (iii) living alone, (iv) reporting a poor relationship with one or more household members, (v) living with three or more children aged <14 years, (vi) loss through death of one or both parents before age 11 years, (vii) separation from either or both parents for $\geqslant 1$ year before age 11 years, (viii) unemployment of spouse/cohabitee, (ix) prior contact with health services for "nerves", (x) low self confidence (determined according to that sub-scale of the Personality Deviance Scale, Bedford & Foulds, 1978).

As shown in Figure 1 those chosen for follow-up included 79 women with a current psychiatric disorder of whom 72.2% were factor-positive, whilst of the remaining group only 45.9% were factor-positive, ($\chi^2_c = 17.79$, df$=1$, $P<0.001$)—a highly significant difference.

At each of the interviews, the subject's psychiatric status was evaluated using a semi-structured clinical interview schedule, the Psychiatric Assessment Schedule (PAS). This was based on the first 40 items of the PSE and selected items from the Schedule for Affective Disorders and Schizophrenia (SADS) (Endicott & Spitzer, 1978).

TABLE I
Follow-up interviews completed by factor and RDC status at initial interview

	RDC Disorder present		No RDC Disorder	
	Factor + ve	*Factor "O"*	*Factor + ve*	*Factor "O"*
No follow-up obtained*	9	4	10	7
First follow-up only	7	0	23	13
Second follow-up only	4	0	4	1
Both follow-ups	37	18	191	87
Total	57	22	228	108
Percentage with at least one follow-up	84.2%	81.8%	95.6%	93.5%

*(Includes refusals, moved away, failure to re-trace; excludes those for whom follow-up was *not* sought).

Information about symptoms obtained through the PAS could be used to generate levels of psychiatric disturbance and tentative diagnostic/syndrome groupings, according to alternative diagnostic schemes.

The PAS provided detailed assessment of each respondent's psychiatric status for the month preceding each interview, as well as seeking information about her clinical state during the inter-interview time periods. If significant symptoms of dysphoric mood (anxiety, loss of interest, or depression) were present the interviewer followed a semi-structured schedule to probe for change-points of illness and to establish accurately when the onset and remission of the episode of illness had occurred. Following the one month assessment, whether this had revealed the presence of symptoms or not, the PAS enquired about the occurrence of specified symptoms in the remaining interview period. For most women, this was about five months, but for those who had missed the first follow-up, this intervening period was about 11 months. Further details describing the PAS are given in an earlier report (Dean *et al.* 1983). Where permission was given, and this was provided by most respondents, each interview was tape-recorded.

The design of the study required that all women who were assigned a psychiatric diagnosis at the initial interview be approached for follow-up. Due to the particular supervision which these interviews required, all were allocated to a group of only five interviewers, including one of the authors (SPS). In advance of these assessments, interviewers were informed which key symptoms had been present at the preceding interview, as this facilitated the assessment of the clinical course of episodes and the dating of major change-points of illness.

Otherwise, all remaining interviews were completed by the team originally trained to undertake the initial survey (for details of this training, see Surtees *et al*, 1983). No additional interviewers were recruited following the start of the study. Because of existing rapport and knowledge of circumstances, an attempt was made to assign interviewers to respondents they had originally seen. However, this was possible in only abut 60% of all follow-up interviews, due to interviewers leaving the study and to the requirement that only a relatively small group undertook the follow-up of respondents fulfilling diagnostic criteria at initial interviews.

The validation procedures adopted for all the interviewers' assessments completed during the follow-up were identical to those applied in the first stage of the study and reported in Surtees *et al* (1983). In brief, if after checking interview material, evidence of psychiatric illness was found, then the audiotape of the interview was listened to and re-rated by staff. Consensus ratings of symptoms were then established by joint discussion between interviewer and a staff rater.

Where respondents had provided interview information from two or three assessments, then two of the authors (PGS and SPS) examined all available clinical material obtained from the interviews. The objectives were to re-evaluate all clinical change points that had been made on restricted information, to date them in relation to each respondent's last interview, and to apply the RDC scheme to all available symptom data. This last objective was fulfilled both under the imposition of all applicable RDC rules, and when two rules were relaxed; viz—the hierarchical relationship between diagnoses, and the elapse of two months stipulated by the scheme to distinguish specific discrete episodes of RDC psychiatric disorder. The results obtained from an analysis of the follow-up data base are presented below.

Results

Of the sample of 576 women initially interviewed, 415 were designated for follow-up. Table I reveals the extent to which we were successful in obtaining re-interviews from this group, divided according to the basis for which they were selected for follow-up.

Whilst at least one follow-up was obtained from 92.8% of the group selected (385/415), significantly more of those women with RDC disorders at initial interview failed to be re-interviewed than those also sought but who were free of RDC disorders at initial interview ($\chi^2_c = 10.75$, df = 1, $P < 0.01$).

TABLE II
Outcome of those followed-up from Sample 'A' (n=66)

Outcome	*Available follow-up period*	
	Six months (frequency)	*One year (frequency)*
Remained ill	6	15
Recovered then relapsed	0	9
Recovered, relapsed then recovered	0	3
Recovered	1	32
Totals	7	59

The result of applying the RDC scheme, unmodified, to all symptoms occurring at any time covered by the follow-up study, together with allowance for the timing of their onset and remission, enabled a summary of the clinical course of all episodes of psychiatric disorder to be made. This summary, together with details of the nature of the disorders will be presented below, separately for Sample 'A' and for Sample 'B'.

Outcome—Sample 'A'

As Table I showed, at least some follow-up information was obtained for 66 of the 79 women who at the time of their initial interview satisfied the RDC for the presence of a psychiatric disorder. A summary of the outcome of this group, by available follow-up duration, is shown in Table II.

Of the group of 66 women, half recovered during the course of their follow-up and remained well until the last interview. The summary of the clinical course of the remainder, shown in the table, revealed 21 (31.8%) to have had a continuous episode since their initial interview, whilst nine (13.6%) recovered from their episode at inception into the study only to succumb to a subsequent one, which was still persisting at their last assessment. Three women recovered from disorders they had described at their initial interview and from a further discrete episode during follow-up. Of those assessed at a one year follow-up, 25.4% (15/59) had remained ill throughout the year, and a further 20.3% (12/59) reported recurrent disorders.

Of the 66 women fulfilling the RDC at initial interview and providing re-interview information, 54 experienced single, and 12 multiple episodes of illness. Application of the RDC scheme as described above, to the data about the symptoms of those with one episode yielded the results shown in Table III.

Under the RDC rules, 75.9% (41/54) were assigned primary diagnoses of depressive disorder and the majority of these, 78.1% (32/41), met the RDC criteria for a major depressive disorder. Few women had primary anxiety disorders. With rule suppression, it was theoretically possible for 43 women, because of their primary diagnoses, to meet criteria for other diagnoses (those with generalised anxiety disorders are already lowest in the hierarchy, and are ineligible). Table III reveals that 34 of these women (79%) described episodes of illness with symptoms which satisfied the RDC for additional diagnoses, all of which (necessarily in this study) were panic/anxiety disorders. Finally the 43 women were further divided according to whether they had recovered during the follow-up, or had remained impaired throughout. Results showed that all 18 chronically ill met the RDC for additional diagnoses, in contrast to 64% (16/25) of those who recovered.

The clinical course of the remaining 12 women who had multiple RDC episodes has already been mentioned. Of the 24 episodes these women experienced, 14 (58%) were depressive in nature, while six had anxiety, and four had panic disorders. Additional diagnoses were theoretically possible for 18 of the episodes: 14 of these actually met the required criteria. Analysis *between* episodes showed that four women had second episodes which changed "diagnostic class"—three women experiencing anxiety/panic disorders following a previous depressive episode, and one vice versa.

Outcome—Sample 'B'

Table IV shows the number of women who had at least one follow-up, the summary of their clinical course over that period, and whether they had been selected because of the presence or absence of any of the putative vulnerability factors.

Of the 46 women who had experienced new episodes, 11 were judged to have onsets which pre-dated their initial interview. Although they were not identified at the first cross-sectional interview as fulfilling the RDC for a current disorder, on the basis of subsequent observations, it was decided that the symptoms which these 11 later described started prior to the initial assessment, even though at the start of the study, these symptoms were of sub-threshold severity. Table IV also reveals that 15.6% of those in the factor-positive group experienced an episode of RDC disorder, in contrast to 11.9% in the factor-zero group—a non-significant difference ($\chi^2_c = 0.5$, df = 1, n.s.).

Table IV showed that 14.4% (46/319) of those followed-up who were free of disorder at initial interview experienced episodes of disorder subsequently. Table V provides the RDC diagnostic breakdown of those episodes.

The primary diagnosis of the majority of episodes (67%, 31/46) was depressive and, as with the results for Sample 'A', most of these were RDC major depressive disorders. However, in contrast to those women with an RDC episode at initial interview, only 53.1% (17/32) of the women experiencing new onsets of disorder (for which, given their primary diagnosis, others were possible) actually fulfilled criteria for subsidiary syndromes.

Episode duration

As the RDC embody inter-episode interval and hierarchical rules, it is particularly important to establish what influence these rules may have upon the duration or primary diagnoses. Within the RDC scheme, it is possible for a relatively short-lived depressive episode to be magnified in

TABLE III

Diagnoses assigned by the Research Diagnostic Criteria (RDC) to those women (n = 54) in Sample 'A' reporting one illness episode

RDC additionally satisfied for:—	*Primary diagnosis*			
	Def./prob. major depressive disorder	*Def./prob. minor depressive disorder*	*Def./prob. panic disorder*	*Generalised anxiety disorder*
Panic disorder and generalised anxiety disorder	8	1	1	0
Generalised anxiety disorder	18	5	1	0
No other diagnosis	6	3	0	11
Total	32	9	2	11

TABLE IV

RDC episode experience during the follow-up for those women in Sample 'B' and by their putative vulnerability factor status

	FACTOR+ve		*FACTOR "O"*		*TOTALS*	
	Frequency	*%*	*Frequency*	*%*	*Frequency*	*%*
No episodes	184	84.4	89	88.1	273	85.6
New episode and recovered	24	11.0	10	9.9	34	10.6
New episode, persisting at follow-up	10	4.6	2	2.0	12	3.8
Total	218	100.0	101	100.0	319	100.0

TABLE V

Diagnoses assigned by the Research Diagnostic Criteria (RDC) to those women (n = 46) in Sample 'B' reporting one illness episode during follow-up

RDC additionally satisfied for:—	*Primary diagnosis*			
	Def./prob. major depressive disorder	*Def./prob. minor depressive disorder*	*Def./prob. panic disorder*	*Generalised anxiety disorder*
Generalized anxiety disorder	16	1	0	0
No other diagnosis	9	5	1	14
Total	25	6	1	14

duration by its occurrence within two months of a much longer term (and hierarchically subsidiary) anxiety or panic disorder. As the timing of all major changes in clinical state were dated in this study, we performed an analysis to determine the extent to which the duration of episodes of hierarchically "subsidiary" diagnoses, through their relative juxtaposition, might have influenced the duration of primary diagnoses.

Table VI contrasts categories of duration of episodes for diagnostically primary, against that of diagnostically "subsidiary" episodes. The table displays the results for those women who initially satisfied the RDC and were followed-up (Sample 'A') and for those free of disorder at the first interview, but subsequently experiencing an onset of RDC psychiatric disorder (Sample 'B').

The table shows that 70.6% (24/34) of Sample 'A' and 76.5% (13/17) of Sample 'B' had primary episodes, the duration of which was largely coincident with that of their subsidiary episodes. Relatively few women (14.7%, 7/34 from Sample 'A'; 17.6%, 3/17 from Sample 'B') had substantial differences in duration between that of their primary and of their subordinate episode. The influence therefore of subsidiary diagnoses to extend the duration of primary diagnoses, appears to be small.

TABLE VI

Relationship between duration of diagnostically primary and subsidiary episodes for those women in Sample (A) and in Sample (B)*

	Duration of "primary" episode	*Duration of "subsidiary" episode*			
		≤ six months	*Six to twelve months*	*> one year*	*No "subsidiary" episode*
Sample (A)	≤ six months	7	1	4	9
	six to twelve months		3	2	2
	> one year	1	2	14	9
Sample (B)	≤ six months	7	3		22
	six to twelve months		3		6
	> one year	1		3	1

*Excludes those ($n = 12$) with multiple episodes during follow-up.

TABLE VII

Nominal and weighted (one month) prevalence of psychiatric disorder determined at each follow-up according to the Research Diagnostic Critiera (RDC). (rates as a %)

Basis for prevalence estimate	*First follow-up RDC diagnosis*	*Second follow-up RDC diagnosis*
Nominal	53/376 14.1%	34/342 9.9%
Weighted[1]	12.7%	8.3%
Weighted[2]	12.9%	9.1%

(1) Simple weighting.
(2) Weighting with allowance for estimated RDC status of losses.

Disease rates

Whilst this report is concerned with aspects of the course of psychiatric disorder commonly found in the general population, attention will be given to the recently documented finding that repeat assessments of psychological health yield prevalence rates of psychiatric disorder that tend to fall with each new assessment (e.g. Henderson *et al*, 1981; Tennant *et al*, 1981).

To examine this question, appropriate allowance has to be made for both the design of the study and for the higher than expected follow-up non-response rate of those women who initially were assigned RDC psychiatric diagnoses, Sample 'A', compared to Sample 'B'. Both nominal and weighted prevalence estimates were therefore determined, based on the immediate one-month pre-interview periods. The results are shown in Table VII.

The one-month prevalence estimate at initial interview was 13.7% and, as can be seen from the table, this is not markedly different from the weighted estimates at first follow-up. However, the results do reveal that whilst little or no decrement in rates occurred between initial interview and first follow-up, the prevalence estimate at second follow-up was over 33% lower than that obtained initially. Henderson considered three main alternatives as possible explanations of his findings. Firstly, that the results could be an artifact produced by a change in response style to succeeding interviews; secondly, that the interviews could have had a therapeutic effect (through assessing symptoms, these were altered, apparently for the better) and, thirdly, that social desirability influenced response. We can advance no additional explanations for our own results. However, whilst our findings suggest confirmation of the findings of others, in view of the high non-response rate, even weighted prevalence estimates corrected for non-response are likely to be inaccurate. These results should therefore be regarded with caution.

The above results take account only of those women meeting the RDC during the month preceding each interview. The next stage of analysis included consideration of the timing of onset and remission, and thereby allowed determination of the recovery rate for Sample 'A' (those who were psychiatrically ill according to the RDC at initial interview). Figure 2 shows the percentage of women at each week of follow-up, within episodes of psychiatric disorder meeting the RDC.

It is clear that initially there was a relatively rapid decline in the proportion of women experiencing an episode, but that after eight months (22 weeks before the end of the follow-up) a plateau was reached with about 40% of those followed-up remaining episodic. This indicated the extent to which significant psychiatric symptoms endure in a cohort of women from the general population. It must be emphasised that in view of losses from this group (13 women had no follow-up, and a further seven only one) and as 65% of those lost had described chronic disorders, then the proportion of women within RDC episodes at any time during the follow-up is likely to be an under-estimate.

The next stage of the analysis determined the (weighted) prevalence of RDC disorder over the follow-up period for those women free of psychiatric disorder at initial interview (Sample 'B'), for each week preceding final interview. Overall rates could not be reliably calculated because of the differential attrition between the two

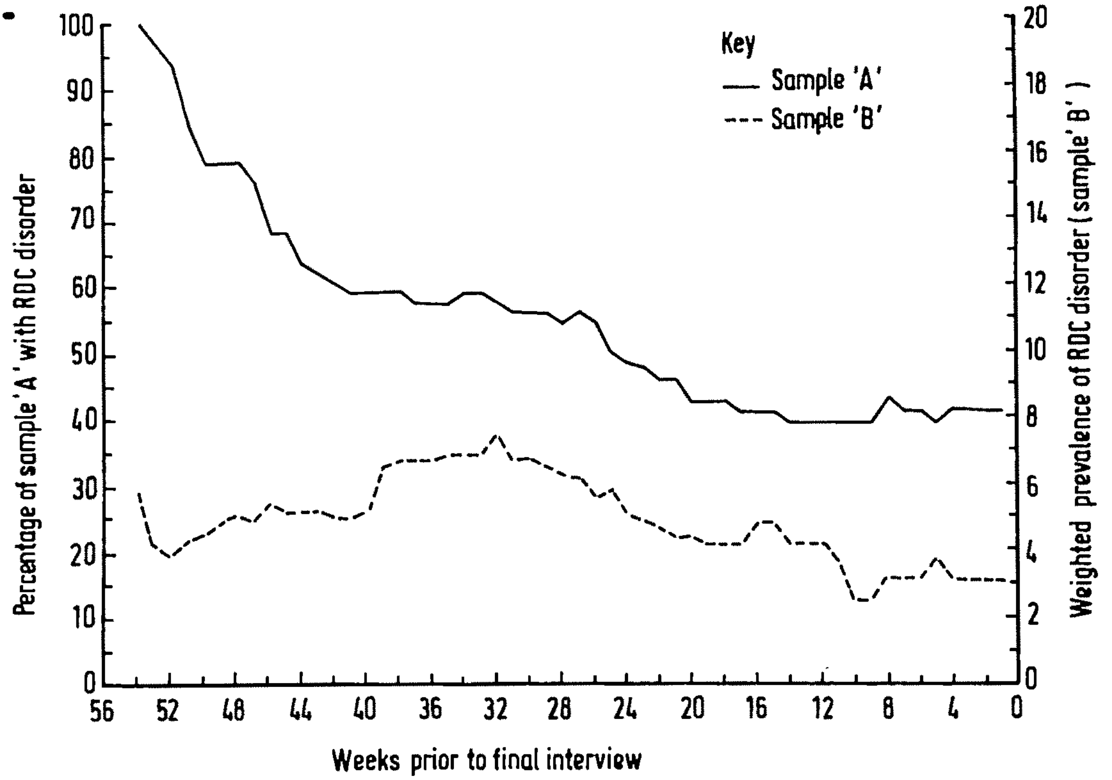

FIG. 2. Presence of RDC disorder among both Sample 'A' and 'B' during the follow-up.

samples (16.5% in Sample 'A' and only 5.1% in Sample 'B'). In spite of the non-significant difference in proportions of new onsets between sub-groups constituting Sample 'B', and shown in Table IV, to reflect the study design, weighting procedures took account of the parent samples of those women free of RDC disorder at initial interview but followed-up on the basis of presence or absence of putative vulnerability factors. The results are also shown in Figure 2.

The figure indicates that prevalence of disorder in Sample 'B' fluctuates between 4% and 7%. It is interesting that the base rate is not at or near zero in this sample, which was constituted on the basis of no evidence of psychiatric disorder at the start of the study. This is because the application of the RDC scheme to information about symptoms obtained from several interviews will inevitably identify some of the subjects as having had a disorder retrospectively, although at the initial cross-sectional interview, they will have been prodromal and not have met the necessary criteria or reached the severity threshold for an RDC disorder. A total of 11 women from Sample 'B' who were retrospectively assigned onsets of illness predating their initial interview had sub-threshold symptoms when first assessed. If these individuals are added to the numerator in calculating the point prevalence of those women meeting our onset critiera at the initial interview, then an estimate of 15.6% is obtained, compared to 13.7% as previously reported.

Epidemiological studies commonly refer to two types of prevalence rates—point-prevalence and period-prevalence. Point-prevalence refers to the number of cases present at a specified moment of time; period-prevalence refers to the number of cases that occur during a specified period of time—e.g. a year. This latter rate therefore includes point-prevalence at the beginning of the specified period plus all new cases that occur during that period. In this study, we have attempted to estimate both point-prevalence (on a random sample, at the cross-sectional interview) and a one-year period-prevalence. The corrected point-prevalence rate at the start of the study has already been mentioned as 15.6% (90/576). Adding all the new cases of RDC disorder that occurred in the follow-up sample to those who were ill at the start of the study produces the total number of women who were cases at any time during the follow-up observation period. Weighting these back (according to their parent sub-groups), we estimate the one-year period-prevalence of RDC disorder at 25.2%. For depressive disorder, the point-prevalence estimate was found to be 11.5% and for anxiety disorder 4.1%. The (one year) period-prevalence estimate of depressive and of anxiety disorder was found to be 17.6% and 7.6% respectively.

TABLE VIII
Consultation history for Sample 'A' and for those from Sample "B" experiencing RDC disorders during observation period (consultation as a per cent)

Consultations	Sample 'A' (n=66) *GP (consultation for "nerves")*	*Psychiatric out-patient*	*Psychiatric in-patient*	Sample 'B' (n=46) *GP (consultation for "nerves")*	*Psychiatric out-patient*	*Psychiatric in-patient*
Ever (before initial interview)	75.8	19.7	13.6	47.8	17.4	4.4
During six months before initial interview	47.0	1.5	0.0	21.7	2.2	0.0
At all during follow-up	45.5	9.1	0.0	69.6	4.4	0.0

The inception rate is a direct estimate of the probability or risk of developing a disease during a specified period of time (Lilienfeld & Lilienfeld, 1980). The limitation of our design precluded calculating inception on the basis of continuously observing a random sample of the population over a specified period of time. Of those in our original sample who were free of RDC disorder, we obtained re-interview information on 64.2% (319/497), representing almost 95% of the sample *chosen* for follow-up. Our estimate of the inception rate of RDC disorder in this group of women (Sample 'B') was determined after appropriate weighting (i.e. whether derived from a sub-group with putative vulnerability factors present or not) and with allowance for the follow-up observation period covered for every woman. This analysis revealed 11.4 new cases of RDC disorder/100 women/year.

Since life history or life-time prevalence rates were not available, "inception" refers here to those who developed the disorder for the first time during the period of observation, some of whom may well have had the disorder in the past. Similarly, those from Sample 'A' (women with current RDC diagnoses at the time of the initial survey) who subsequently recovered and then relapsed after the minimum inter-episode interval, as specified by the RDC, are not included in the rate mentioned above. We had 12 women from Sample 'A' who developed more than one episode. When these women were included in the calculation, again with appropriate allowance for weighting and observation period, the incidence rate of episodes was found to be 12.6 new episodes of RDC disorder/100 women/year.

Contact with health services

This paper has so far suggested that those disorders detected amongst our community sample are neither trivial in nature (most meeting the RDC for major depressive disorders) nor transient in duration (many lasting for more than one year). To examine the contact with psychiatric services which these women had sought, their responses to questions asked at initial interview and at follow-up were analysed. The results are shown in Table VIII.

None of the women meeting the RDC for a disorder, either during the six months preceding initial interview or during the follow-up period, entered psychiatric care as an in-patient. When psychiatric out-patient consultations were considered for the same time-periods, then seven women from Sample 'A' consulted and only two women (4.4%) from Sample 'B', one woman consulting during both time periods. It is clear that whilst the burden of treatment was retained by general practitioners, over half of Sample 'A' and 30% of those with disorders in Sample 'B' sought no help at all from these agencies during the follow-up observation period.

Discussion

In spite of the availability of reliable case finding techniques and renewed interest in the epidemiology of mental disorders outside treatment settings, very few attempts have been made either to describe the natural history of such disorders, or to establish their inception in sub-groups of the population. This study illustrates some of the advantages and difficulties inherent in attempting to conduct a prospective, longitudinal study to achieve these objectives.

The research design was adopted primarily to investigate the differential vulnerability of women in the general population to psychiatric disorder, rather than to provide prevalence and inception estimates. Our design, compounded by losses from chosen follow-up samples, may restrict the usefulness of disease rates based upon episodes of illness detected during the follow-up period. These reservations concerning both the design and methodology must be borne in mind when interpreting our findings.

Our adoption of the RDC in association with a repeated symptom assessment method enabled us to define and describe all episodes of illness occurring during the study period. However, the integration of information obtained from several interviews was only possible through making arbitrary rules about the onset and offset of episodes. This was achieved through discussion between the authors and the interviewers on the basis of all available symptom information concerning each respondent and by relying on the accounts given in response to a semi-structured interview schedule, designed to document the clinical course.

As we classified morbidity according to a restricted range of RDC (dysthymic) disorders, it is possible that we failed to identify certain other conditions in the community. A study undertaken by Weissman & Myers (1980) in a community study in New Haven provides a basis on which to examine the likely consequence of not assessing certain diagnoses. They obtained an overall point prevalence rate of 18.9% for women with a diagnosis of *any* functional psychiatric disorder according to the RDC scheme, and found that more than one diagnosis was allocated to 5.1% of the sample of 291 women. Their published rates for conditions which we did not assess (1.7% alcoholism, 1.4% bipolar disorder, 1.4% drug abuse, 0.3% antisocial personality disorder, 0.3% unspecified functional psychoses, and 0.0% schizophrenia) suggest that our false negative rate should not have exceeded about 4% of our total sample. As over 5% of the New Haven sample were assigned more than one diagnosis, it is likely, therefore, that some of those women in our study who had sufficient symptoms to be considered as psychiatrically ill according to the RDC had relatively poor diagnostic specificity. For example, it is possible that if our psychiatric assessment had dealt with the requirements of all the RDC diagnostic categories, a small group of our "cases" would have changed their labels (say from generalised anxiety disorder to alcoholism) or might possibly have achieved a better clinical description (from generalised anxiety disorder to generalised anxiety disorder *and* antisocial personality).

The majority of depressive episodes identified in this study also met criteria for subsidiary diagnoses, revealing the frequent co-existence of depressive and anxiety symptoms in conditions found in the community—a finding also frequently reported from hospital based studies (e.g. Paykel, 1971). Attempts therefore to delineate the two symptom patterns as independent categories for the purpose of testing aetiological hypotheses would be unrealistic if based upon community samples.

Of the women who had one episode of illness during the study, 54% from Sample 'B' and 60% from Sample 'A' fulfilled the criteria for major depressive disorder according to the RDC. Apart from depressed mood (rated according to PSE criteria) they experienced at least four other symptoms of sufficient severity for the episode of illness to have led to a significant impairment in their functioning. Whilst the minimum duration of symptoms for achieving a diagnosis was one week, this study revealed that half of those subjects followed-up were suffering from chronic or recurrent conditions. Results from general practice based studies, which suggest that such conditions also frequently follow a fluctuating and chronic course, are consistent with this finding (e.g. Cooper *et al*, 1969; Mann *et al*, 1981). Although the severity of depressive disorders assessed in community studies is lower than those presenting to the psychiatric services (where psychotic symptoms or behavioural features are more often associated with clinical presentation), our findings suggest that it would be both inappropriate and misleading to classify them as either "minor" or transitory forms of "demoralisation". The issue remains as to whether a diagnostic taxonomy appropriate to psychiatric conditions found in hospital settings is usefully transferable to those in a community setting.

Most community surveys report only point prevalence rates of disorder and in consequence, this limits comparison with disease rates observed in surveys of consulting populations (Goldberg & Huxley, 1980). In this study, we calculated period-prevalence rates on the basis of longitudinal observation: our one-year period/prevalence rate for RDC disorders was found to be 25.2% (almost double that of the one month rate, 13.7%, estimated from the first cross-sectional interview). This can be contrasted with results obtained from a survey in Camberwell undertaken by Brown *et al* (Brown & Harris, 1978). They obtained a one-year rate of 16.6%, based on all definite cases in the year, and a rate of 35.6% when all borderline conditions were aslo included.

In other studies, inception rates for affective disorders in the community have been calculated either by longitudinal observation or on the basis of retrospective information obtained at a single interview. A study of a rural community in Sweden (Hagnell *et al*, 1982) calculated the frequency and risk of depression on the basis of three interviews that spanned a 25-year period (1947–1972). By using non-standardised clinical observation and historical information, the annual inception of depressive disorders (with severe, medium and mild impairment) among women was estimated at 4.1/1000, based upon the first ten years of this period and 7.7/1000 over the last ten years. Two studies (Hallstrom, 1973; Brown & Harris, 1978) which covered a one-year period by a retrospective single interview method obtained much higher figures. The annual inception rate of depressive disorders among women in Gothenburg was estimated to be 61.75/

1000 and in Camberwell 78.6/1000. When *onsets* of both definite and borderline cases of all conditions are included, and if recurrent episodes are counted as new episodes, then the Camberwell rate almost doubles to 148.5/1000 per year. The rate we obtained, 126/1000 per year, again based upon onsets of all diagnostic categories is closer to this latter figure. To our knowledge, this study is the first to calculate an inception rate among the general population using a longitudinal cohort design and standardised diagnostic methods.

Recent surveys (Brown & Harris, 1978; Weissman & Myers, 1980; Wing *et al*, 1981; Roberts & Vernon, 1982) have found that substantial numbers of individuals with psychological symptoms in the community seek medical advice for their problems. In this study, consultation estimates reflected the proportion of women seeking help for "nerves", and did not include all primary care attendances. Amongst the group unwell at initial interview, 47% had consulted their GP for their psychiatric symptoms in the preceding six months. A consultation rate of 68% was obtained amongst 76 depressed women who were identified during a community survey in Camberwell (Brown & Harris, 1978). However, this latter rate includes all consultations for symptoms made at any time during their illness episodes, and therefore will be based upon a longer pre-interview time period than our own. Weissman & Myers (1980) found that 25% of their sample with RDC dysthymic disorders in the community, consulted a general medical or mental health professional for emotional problems during the year preceding interview. In the present study, those who were ill at the first interview had, as expected, a higher consultation rate in the six months before their interview, when compared to Sample 'B' who were well at that time. During the follow-up period, however, more of Sample 'B' (70%) sought help from their family doctors, in contrast to 46% of Sample 'A'. One possibility is that consultation with GPs is more likely around the time of onset of the illness, but that medical advice is less likely to be sought once the symptoms become chronic.

This study has been an attempt to describe the epidemiology of affective disorder in the general population. Whilst our results reveal the nature and form of the disorders, they provide no solution to aetiological or service issues, but could be seen as providing a sound basis upon which new research questions may be formulated.

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*P. G. Surtees, BSc, MSc, PhD
S. P. Sashidharan, MB, BS, MPhil, MRCPsych

MRC Unit for Epidemiological Studies in Psychiatry, University Department of Psychiatry, Royal Edinburgh Hospital, Morningside Park, Edinburgh EH10 5HF

C. Dean BA, MD, MRCPsych, *Consultant Psychiatrist, Department of Psychiatry, Manchester Royal Infirmary, Manchester*

*Correspondence

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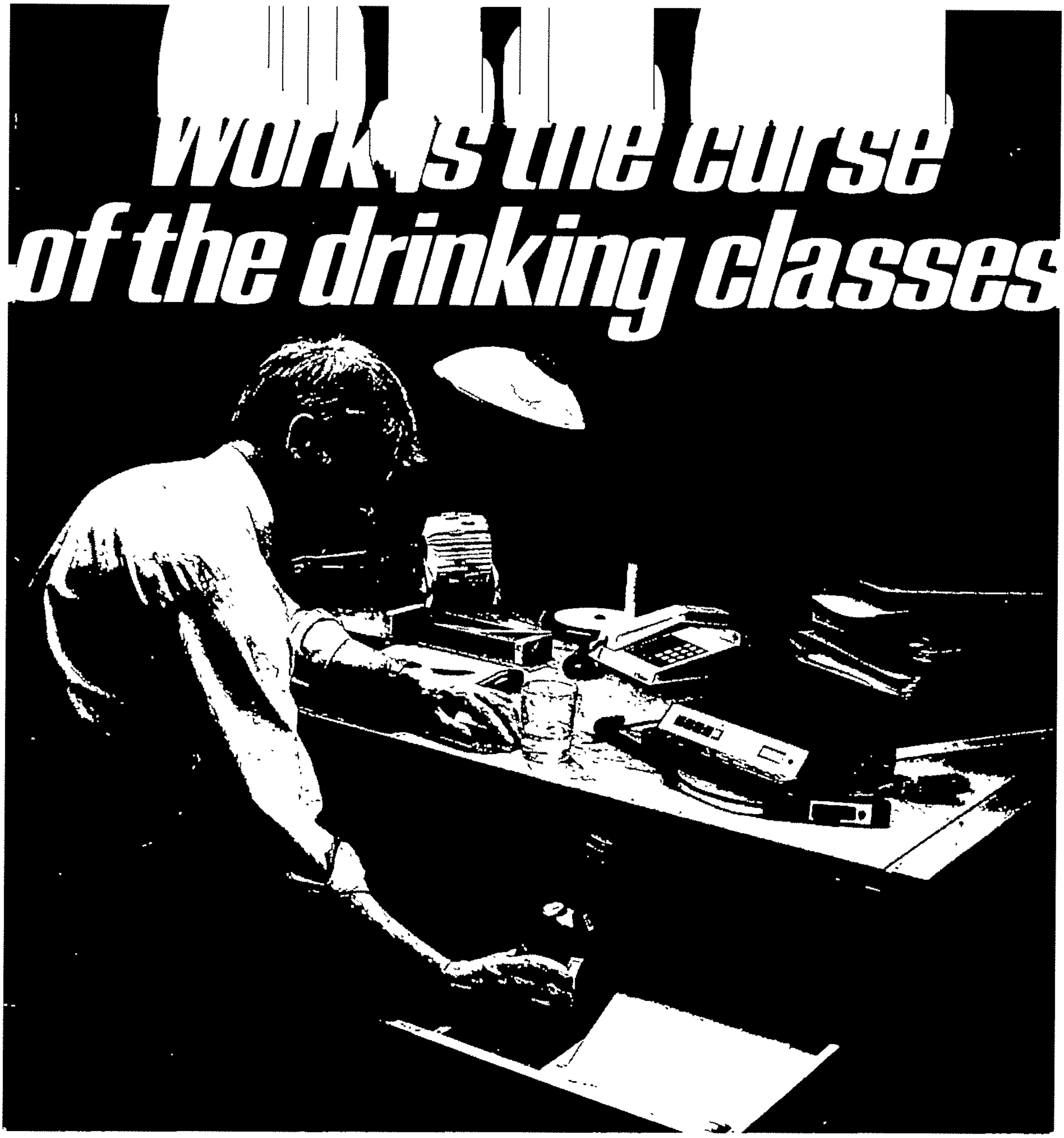

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Radio Receptor Assay of Serum Neuroleptic Levels in Psychiatric Patients

JANET KRSKA, G. SAMPATH, A. SHAH and S. D. SONI

The radioreceptor assay for the measurement of neuroleptic drugs in serum has been used to study the relationship between dose and serum level in schizophrenic patients receiving these drugs. The assay was found to be reproducible and capable of detecting neuroleptics in the sera of patients receiving a range of both oral and depot drugs, with the exception of trifluoperazine spansules. Linear correlations were obtained between daily dose and serum level for each drug both in individual patients on different doses and between patients on a stable dose. Extrapyramidal side effects were related to the serum neuroleptic level within, but not between, patients. The assay may be of use in clinical practice, including the assessment of compliance or poor response to neuroleptics.

The usefulness of drug level monitoring has been well established for lithium and anticonvulsants and can also be helpful in tricyclic antidepressant therapy (Amsterdam *et al*, 1980). In recent years a large degree of interest has arisen in the measurement of neuroleptic concentrations in body fluids of patients undergoing treatment with these drugs. The main reasons for this are the current availability of a number of methods capable of measuring neuroleptic drug levels, the apparent lack of relationship between dosage and clinical effect and the desire to optimise drug therapy.

Many studies have been undertaken to determine the value of neuroleptic drug level measurement in relation to antipsychotic effect and the appearance of extra-pyramidal side effects, including tardive dyskinesia. However, the results of these studies are conflicting, many show a complete lack of relation of clinical effects to blood levels (Kolakowska *et al*, 1976; Wiles *et al*, 1976), while others vary in their degree of success in demonstrating the existence of such relationships (e.g. Sakalis *et al*, 1972; Rao *et al*, 1980). Two possible factors may contribute to this lack of agreement, namely, the large variation in study design and the different methods of measuring neuroleptic levels. Study design is a particularly difficult problem in psychiatry which results in poor comparability, while the numerous methods of detection of neuroleptics in blood vary greatly in what is actually measured.

Many methods measure only the parent compound or a few additional metabolites. This may not be of great value for drugs such as chlorpromazine which have many metabolites, an unknown number of which may also be biologically active (Sakalis *et al*, 1973; Mackay *et al*, 1974). The radioreceptor assay (RRA) method of Creese & Snyder (1977) seems to offer a more relevant approach as it measures the amount of drug(s) in the blood which bind to dopamine receptors obtained from mammalian brains. Since blockade of such dopamine receptors is the only property common to neuroleptics which correlates with their clinical potency (Seeman *et al*, 1976), measurement of dopamine-blocking activity would seem to be theoretically superior to simple measurement of parent compound in blood samples for clinical studies. Indeed, most of the workers using the radioreceptor assay have had some success in their search for a "therapeutic window" for neuroleptics (Calil *et al.* 1979; Cohen *et al*, 1980a; Dunlop *et al*, 1982; Tune *et al*, 1980).

The radioreceptor assay was therefore set up following a slightly modified method (Cohen *et al*, 1980b) to study further the relationships between dosage, serum levels and clinical effects. This paper describes the assay as used here and the studies carried out on the effect of dosage on the serum levels as measured by this method.

Method

Radioreceptor assay for neuroleptics

The radioreceptor assay method as described by Cohen *et al*, (1980b) uses calf caudate nucleus as a source of dopamine receptors. Calf brains were obtained from a local abattoir, the caudate nuclei dissected out, weighed and homogenised in 20 volumes of 50 mM Tris HCl buffer, pH 7.7 at 25°C, using an Ultra Turrax homogeniser. The suspension was centrifuged at 39000 g for 20 minutes, the pellet resuspended in a further 20 volumes of buffer and centrifuged again. The final pellet was homogenised in 10 volumes of special assay buffer, containing 5 mM

Na_2EDTA and 1 mM ascorbic acid. The suspension was then frozen in 2.5 ml aliquots at −20°C.

To perform an assay, the 2.5 ml of suspension, once thawed, was diluted to 10 ml with fresh assay buffer, homogenised for 10 seconds and further diluted to 20 ml. ^3H-spiroperidol (28.4 Ci/mMol, New England Nuclear) was diluted to 1 nM with distilled water. (+)−butaclamol, used to define specific binding to dopamine receptors, and all drugs, were diluted with assay buffer. Glass incubation tubes, kept at 4°C, received 150 µl (+)−butaclamol (for non-specific binding, final concentration 1 µM) or 150 µl haloperidol (for standard curve, final concentrations 3, 5, 10, 20, 40 and 60 nM) or 150 µl assay buffer (for total binding and unknown serum samples), 150 µl serum (pooled normal or patient sample), 300 µl ^3H-spiroperidol (final concentration 0.33 nM) and 300 µl tissue suspension (final concentration 3.75 mg tube), the total volume being 900 µl.

After mixing, the tubes were incubated for 15 minutes at 37°C, then the mixture filtered rapidly under constant vacuum (500 mm Hg) through Whatman GF/B filters in a Millipore manifold with 3 × 5 ml rinses of ice-cold Tris HCl buffer. The filters were then transferred to scintillation vials, dried in a hot air oven for 2 hours, 4 ml scintillation liquid (toluene, scintillation grade, containing 5 g/l PPO, and 0.1 g/l POPOP) added and counted for 10 minutes per vial in either an LKB 81000 or Rack Beta liquid scintillation counter.

Total ^3H-spiroperidol binding was calculated as a percentage of the total activity per vial (determined by counting 300 µl ^3H-spiroperidol solution plus a filter). Specific binding to dopamine receptors was calculated as the difference between counts in the presence or absence of (+)−butaclamol. The standard curve for inhibition of specific binding by haloperidol was converted to a straight line using a log-logit plot and neuroleptic activity in samples (expressed as neuroleptic units, N.U.) calculated using a radio-immuno-assay program. One neuroleptic unit is defined as the degree of dopamine receptor blockade produced in the assay by a 1 nM solution of haloperidol.

Patients

Eight stable, hospitalised chronic schizophrenic patients volunteered for study of serum levels in relation to dosage of neuroleptics. They received a single daily dose of chlorpromazine or haloperidol, which was increased at weekly intervals up to a maximum of 1200 mg chlorpromazine or 120 mg haloperidol or until side effects developed. The drug was then either reduced stepwise at weekly intervals or continued at an appropriate dose according to the judgement of the clinician. Blood samples were taken after one week at each dosage level, approximately 12 hours after the last dose, at the same time of day. Patients were also rated for clinical state using the Brief Psychiatric Rating Scale (BPRS) (Overall & Gorham, 1962) and side-effects using the Extra-Pryamidal Symptoms (EPS) Scale (Simpson & Angus, 1970) at the same time as samples were taken.

Single blood samples were also obtained from a large number of patients receiving a single neuroleptic to determine relationships between dose and serum level in different patients; and from patients receiving other psychotropic drugs to test for interference in the assay.

Sample collection

Ten ml of venous blood were collected into a red-stoppered tube (Brunswick) and left to clot for at least 60 minutes. The tubes were centrifuged for 10 minutes and the serum obtained transferred to glass tubes (three aliquots per sample) which were then frozen at −20°C until assayed 1–12 weeks later.

Results

Properties of the radioreceptor assay

The total amount of ^3H-spiroperidol bound to the caudate tissue in the presence of 150 µl pooled normal serum varied only slightly between batches from 19.6 ± 2.5 to 21.3 ± 3.0 (mean ± S.D.) percent of the total added, over a period of nine months. The proportion of the spiroperidol which was bound specifically to dopamine receptors was also fairly constant between batches, ranging from 83.1 ± 1.3% to 85.4 ± 2.8%.

Dose response curves for inhibition of spiroperidol binding were obtained for several neuroleptics and other drugs, in the presence of 150 µl serum. The IC_{50} concentrations compare well with those found by other workers for this system. Procyclidine, lithium and diazepam did not inhibit binding even at high concentrations and serum samples from patients receiving either these drugs or other benzodiazepines, anti-convulsants, imipramine, mianserin or hydergine did not interfere in the assay. One out of five samples from patients receiving amitriptyline and one of three on dothiepin did show a small amount of inhibition of spiroperidol binding. Haloperidol was chosen as the internal standard for assay of serum neuroleptic samples since it is chemically stable and is also used as a standard for this method by most other workers.

The standard curve was reproducible between batches of caudate tissue, the IC_{50} ranging from 9.17 ± 1.5 nM to 10.47 ± 1.2 nM. The limit of sensitivity of the assay (lower detection limit) can be defined in two ways; as that concentration distinguishable from the mean of the total binding in the absence of drugs less two standard deviations or as 15% inhibition of specific ^3H-spiroperidol binding. For this assay, allowing for dilution of the sample, the limit of sensitivity for haloperidol by the first method is 7.9 nM (2.96 ng/ml) and by the second method 7.3 nM (2.73 ng/ml).

Recovery of haloperidol from serum was assessed by adding known concentrations to pooled normal serum and assaying, either immediately or after freezing and re-thawing. Intra and inter-assay variation was assessed by assaying these known samples repeatedly up to ten times within one assay and in separate assays. The results are shown in Table IA. Mean recovery of haloperidol was 91.5 to 115.3%; in general a slight over-estimation occurred. The reproducibility of the assay, shown by the coefficient of variation, was similar both within and between assays.

TABLE I

Reproducibility of radioreceptor assay for neuroleptics

A. Known samples

1. Within assay

Conc. added	Conc. recovered		% recovered		CV%
nM	x̄	SD	x̄	range	
15	16.61	2.33	110.7	86.9–138	14.02
30	31.38	2.63	104.9	93.6–116	8.38
60	54.95	6.85	91.5	74.9–111.3	12.5
90	95.1	14.4	105.7	83.2–138	15.16
150	153.62	21.1	102.4	83.9–122	13.7

2. Between assay

Conc. added	Conc. recovered		% recovered		CV%
nM	x̄	SD	x̄	range	
15	17.36	3.48	115.7	68.5–139.5	20.0
30	34.6	3.6	115.3	94.1–122	10.4
60	64.4	5.99	107.3	90.8–120.1	9.3
90	97.5	13.55	108.3	80.5–124.7	13.9
150	151.6	7.6	102.4	95.9–110.2	4.8

B. Clinical samples

Serum level range (Neuroleptic units)	Mean interassay CV%	*n*
0–10	38.3	23
10–20	25.7	28
20–50	18.2	42
50–80	14.0	17
80–100	17.1	8
>100	17.7	9

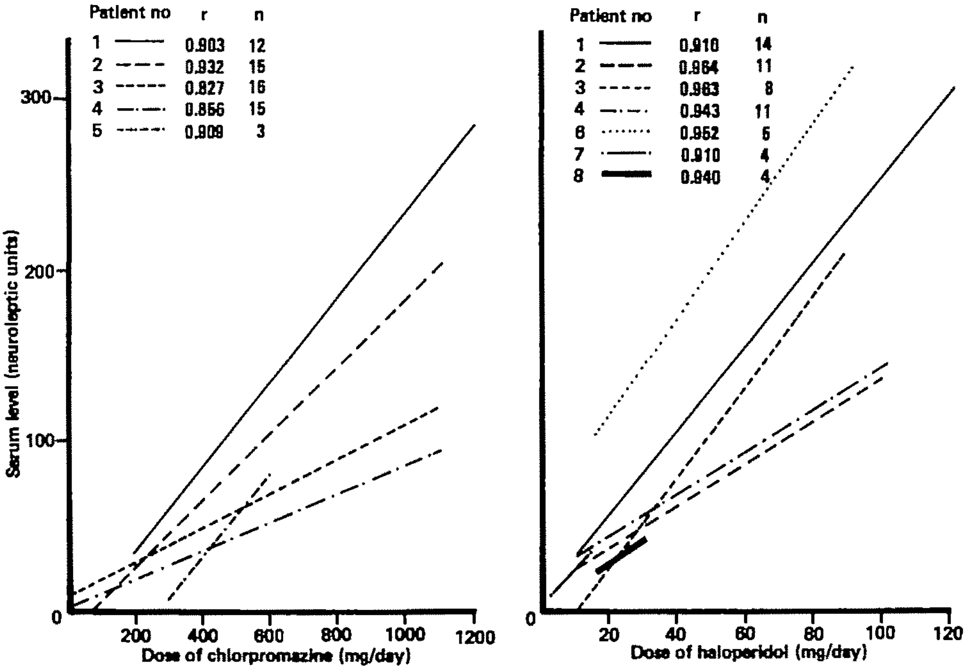

FIG. 1. Correlations between dose and serum level in individual patients. r = Pearson's correlation coefficient. *n* = no. of samples per patient.

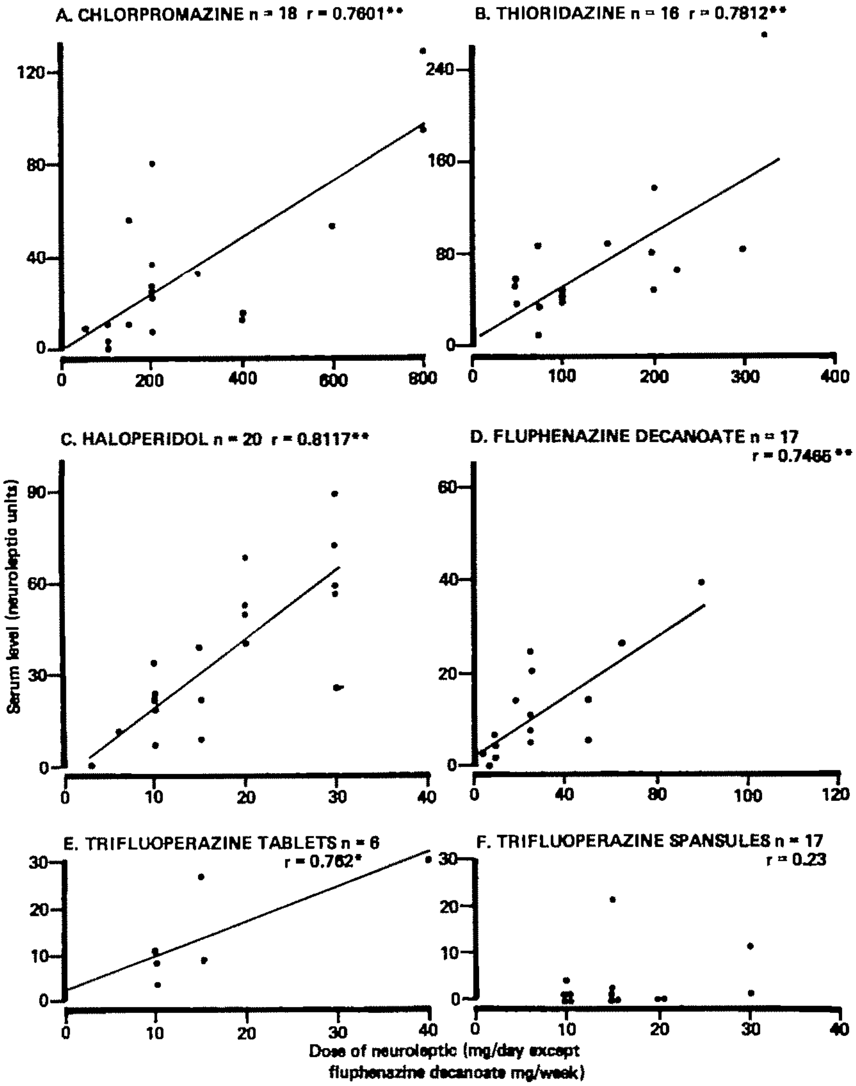

FIG. 2. Correlations between dose and serum level between patients for various neuroleptics $^*P<0.05$, $^{**}P<0.0005$.

Reproducibility of clinical samples was calculated as the mean coefficient of variation for all samples assayed at least three times within the ranges of serum levels shown (Table IB). The average correlation between values obtained for clinical samples assayed on more than one occasion was good ($r=0.947$). No reduction in neuroleptic activity was found on storage of samples for up to six months.

Dose/serum level correlations

Within patients

The relationship between daily dose and serum level in individual patients on an increasing dosage regime only was studied in 3 patients on haloperidol and 1 on chlorpromazine. Four further patients received both increasing and decreasing dosage regimes of both drugs.

In all patients a highly significant linear correlation was obtained between daily dose of drug (mg/day) and serum neuroleptic level. In those patients who received increasing and decreasing doses of drugs, serum levels achieved were similar on both occasions each patient received each dose. The regression coefficients were thus not significantly different between the two regimes, with the possible exception of one patient, who, when taking haloperidol, also received lorazepam in constant dosage during the reducing phase ($P>0.1$). Consequently, the data from increasing and decreasing doses in these patients was combined. In two of

TABLE II
Correlations between dose, serum level and extrapyramidal side effects

Drug	*No. of patients*	*Correlation coefficients*	
		Dose/EPS	*Serum level/EPS*
Chlorpromazine	Those with side effects (2)	0.9224***	0.8499***
	All patients (5)	0.5213*	0.2096
Haloperidol	Those with side effects (5)	0.9397†	0.9724†
	All patients (7)	0.5889**	0.5307

*$P<0.05$ **$P<0.01$ ***$P<0.005$ †$P<0.005$.

the patients on haloperidol, serum levels appeared to level out at doses of 80 mg/day and above, however, linear regression data are shown to enable comparisons to be made with other patient data. The regression lines and correlation coefficients for individual patients are shown in Figure 1. The slopes of the regression lines and serum levels achieved varied considerably between patients; however, the pattern of variation between patients who received both drugs was not consistent.

Between patients

Samples obtained from 87 patients receiving a single neuroleptic were also assayed to determine whether similar relationships between dose and serum level could be shown to exist between patients.

Linear correlations were found for patients on chlorpromazine, haloperidol, thioridazine and fluphenazine decanoate. Again there was a large variation in the serum levels obtained between different patients on the same dose. The results are shown in Figure 2. Patients receiving trifluoperazine spansules generally achieved very low serum levels and no relation to dosage could be established. The possibility that this could be due to the use of a slow release preparation was examined by measuring levels in 6 patients receiving tablets. The serum levels achieved in these patients were in all cases higher than those after slow-release capsules and did show a linear relationship (Figure 2).

Serum level/clinical effect correlations

Extra-pyramidal side effects were found to be present in only 2/5 patients on chlorpromazine, but in 5/7 patients on haloperidol. In those patients who experienced side effects, they were found to be significantly related to both daily dose of drug and serum level (Table II). The correlation between EPS score and serum level is shown for those patients in Figure 3, which also illustrates the much higher scores in patients receiving haloperidol than those on chlorpromazine. When data was combined for all patients including, those who had no side effects, the relationships were less marked (Table II), as one particular patient was able to tolerate very high doses of drugs, and despite achieving extremely high serum levels, experienced no side effects. There is thus no clear relationship between side effects and either dose or serum level between patients.

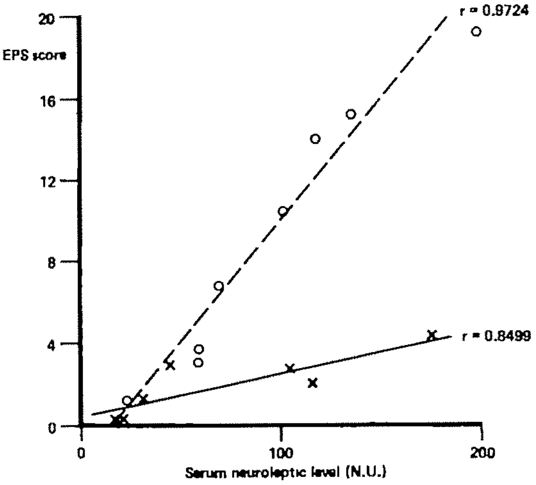

FIG. 3. Extrapyramidal side effects in relation to serum levels of: (x) 2 patients on chlorpromazine, (O) 5 patients on haloperidol. Each point represents the mean value at one dosage level.

The clinical state of the patients as assessed by the BPRS did not show any major changes despite the large alterations in dosage and variations in serum level. This was not so surprising in view of the fact that these were all chronically ill patients who had been stable for several years. The only notable change was in increase in the BPRS score of one patient at a time when his serum level was particularly high.

Discussion

The radioreceptor assay has been found to be a cheap and easy method of measuring serum neuroleptic levels. The reproducibility of the technique, though not as good as that sometimes achieved by other methods, such as radio-immunoassay (RIA) or high pressure liquid chromatography (HPLC) is adequate for clinical use, at least for patients receiving oral medication. At lower concentrations, towards the limit of sensitivity of the assay, reproducibility is not as good. Since these concentrations are commonly found in patients receiving depot preparations, the assay may not be as suitable for studying these drugs. The assay method was found to have better sensitivity and reproducibility than that of Lader (1980); this may be due to the use of a frozen rather than freeze dried preparation of dopamine receptors.

The ease with which correlations were obtained between daily dose and serum level amongst patients receiving different doses of neuroleptics suggests that the radioreceptor method may be particularly suitable for this type of study. Previous studies have generally been unable to show good correlations between dose and serum level for chlorpromazine using gas liquid chromatography (GLC) methods (e.g. Rivera-Calimlim *et al,* 1973); however, such correlations have been consistently found for haloperidol (e.g. Rowell *et al,* 1981). This may be a reflection of the importance of measuring metabolites in these studies, as haloperidol, unlike chlorpromazine, is not extensively metabolised.

A similar situation is apparent among the large number of studies performed in an attempt to relate blood levels to clinical effects by measuring parent drug alone. For chlorpromazine, this has proved to be difficult, the greatest degree of success being achieved by Rivera-Calimlim *et al* (1973, 1976), who suggested plasma levels of 50–300 ng/ml were associated with clinical improvement. Other workers have generally not found such relationships (e.g. Kolakowska *et al,* 1976). Two groups of workers have independently proposed a therapeutic window for serum/plasma levels of haloperidol (Magliozzi *et al,* 1981; 8–18 ng/ml; Smith *et al,* 1982; 5–14 ng/ml). These studies suggest that it is easier to show a correlation between clinical effects and serum levels for drugs which do not have many active metabolites, and that the radioreceptor assay may be a more relevant technique for such studies.

Many workers have used the method in clinical studies involving various neuroleptics. It has been suggested that levels of dopamine-receptor-blocking-activity would be similar in all patients, irrespective of the neuroleptic, and two groups of workers have found relationships between blood neuroleptic levels and clinical response on this basis (Tune *et al,* 1980; Dunlop *et al,* 1982). Other workers have however found that each drug results in a different range of blood levels, as measured by this method (Cohen *et al,* 1980c; Calil *et al,* 1979) and this is supported by our findings. Cohen *et al* (1980a) found a minimum plasma level of thioridazine of 2000 nM was necessary for clinical effect, while that for fluphenazine was found to be 5 nM (Harris *et al,* 1982). A good relationship between serum level and clinical state for haloperidol has also been described using RRA (Calil *et al,* 1979), but by no means universally (Smith *et al,* 1980). Brown *et al* (1982) used the radioreceptor assay to measure serum neuroleptic levels in chronic patients and found that those with low levels relapsed.

It seems, therefore, that the radioreceptor assay is useful for clinical studies, although much more work is needed before monitoring of serum neuroleptic levels could become routine in clinical psychiatry. However, there are immediate applications of the technique which could be of value. The correlations obtained between dose and serum neuroleptic level can be used to assess both compliance and poor response, since it may be apparent from a single sample whether a patient is taking medication or achieving low serum levels. Thus, even without a well-defined therapeutic window, it may still be possible to monitor patients who present problems of poor clinical response.

The data suggests that there is a relationship between serum levels and side effects in individual patients. Each patient had a different "threshold" serum level above which side effects developed, and when serum levels fell below this point side effects disappeared. However, in these patients, dose was similarly related to side effects, hence knowledge of the "threshold" serum level would not be superior to knowledge of the dose. Only one group of workers so far have found correlations between serum levels and side effects between different patients (Smith *et al,* 1980); perhaps this may be due to the variations in threshold described here.

It is possible that a similar situation may be found to exist for the antipsychotic effect of neuroleptics, namely that each patient has a different threshold, although the studies described above suggest otherwise. If a therapeutic window or a minimum effective serum level can be established for neuroleptics, then measurement of serum levels could be used as an independent, objective means of optimising drug therapy. Studies are at present under way in our laboratory to investigate this issue.

In conclusion, the radio-receptor assay is not only a useful method for undertaking the research necessary to establish therapeutic levels, but may be a simple and cheap method of monitoring serum levels routinely.

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Janet Krska, BSc, MPS, PhD, *Research Fellow*
G. Sampath, MD, MRCPsych, *Senior Registrar*
A. Shah, MB, BS, *Research Registrar*
*S. D. Soni, MD, PhD, FRCP, FRCPsych, *Consultant Psychiatrist*

Department of Psychiatry, Salford Health Authority, Prestwich Hospital, Prestwich, Manchester M25 7BL

*Correspondence

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Hospital Doctors' Management of Psychological Problems

RICHARD MAYOU and E. B. O. SMITH

Psychological and social difficulties are common amongst both medical and surgical patients, but psychiatrists are able to see only a very small proportion, and though hospital doctors have the main responsibility for psychological treatment, very little is known of what they actually do. Physicians and surgeons in Oxford answered a questionnaire on their attitudes and clinical practice: virtually all believed that emotional care is important, but what they do and what they would like to do in the assessment, treatment, and referral of their patients varied widely. There were associations with the extent of responsibility for chronic care, speciality, and seniority.

Emotional disorders, organic mental states, and drinking problems (Editorial, 1981) are all common in general hospital wards and clinics. A small proportion of patients are referred to psychiatrists, but most assessment and treatment is provided by physicians and surgeons and by their clinical teams. Although they have to be able to manage the emotional and organic consequences of physical illness and to identify primary psychiatric illness, little is known of how such doctors do this. In surveys of Detroit general hospitals (Fauman, 1981; 1983) consultant staff estimated that 14% of their patients had significant psychiatric problems and that they spent 17% of their time treating such problems. Other American reports conclude that junior hospital doctors have an unsatisfactory knowledge of psychiatry (Cohen-Cole *et al*, 1982; Berkowitz, 1981) and that prescription of psychotropic drugs is often excessive and unsystematic (Davidson *et al*, 1975; Salzman, 1981).

We need research in the general hospital which is similar to that described in general practice (Goldberg & Huxley, 1980), and this paper describes a first step—a detailed survey of hospital doctors' views on the management of their patients' psychological problems. There can be no right or wrong answers; both because it is uncertain what psychological and social care hospital patients need, and also because there are many ways of providing it. Hospital doctors have a special responsibility for it, but good care also involves nurses, other members of the clinical team, and general practitioners.

Method

We sent questionnaires to all those listed in the Oxford General Hospitals' list of clinical staff, but excluded paediatricians and pre-registration housemen. The first part of the questionnaire, adapted from that used in general practice by Shepherd *et al.* (1966), was a list of general attitudes to psychosocial care (strongly agree, agree, uncertain, disagree, strongly disagree); questions on referral to psychiatrists were based on those used by Mezey & Kellett (1971). The remaining sections of the questionnaire requested factual information on methods of assessment and treatment. The questionnaires were completed anonymously, but were numbered so that we could send a shorter questionnaire to those not replying. Of 218 doctors circulated, 194 (88%) replied, including 94% of consultants, with all except one completing the full questionnaire, and 84% of junior staff, with 82% of these completing the full questionnaire. There were no significant differences between replies to the full or shorter questionnaire for any of the questions; 62 doctors responded to a request for comments. Chi squared was used for statistical analysis.

Results

General attitudes

Of Oxford hospital doctors, 77% believed that psychological factors can influence the course and outcome of physical disorder; all agreed that emotional care is an important part of hospital medicine, and two-thirds said this enhanced the interest of their work. However, there were diverse views about what hospital doctors can and should do in everyday practice. Thus, one-third felt that the management of social and emotional difficulties of inpatients was definitely a medical responsibility, a fifth said it was a nursing responsibility, and the remainder felt it should be shared.

We also asked about common problems (Table I). Three-quarters of the doctors felt they should treat acute organic mental states, but far fewer felt any responsibility for the management of depression, chronic drinking problems, or emotional care of the dying. Lack of time was seen as a considerable problem, and almost half (46%) said that it is impractical for hospital doctors to assess and treat emotional problems; 78% would have liked more time to talk to their patients.

TABLE I

Responsibility for common types of psychological problems (%)

Hospital doctors have the major responsibility for the management of the following problems:	*Agree strongly*	*Agree*	*Uncertain*	*Disagree*	*Disagree strongly*
Depression	9 (5)	36 (21)	51 (20)	74 (41)	5 (3)
Acute organic	30 (17)	104 (59)	22 (13)	18 (10)	1 (1)
Overdoses	12 (7)	51 (29)	57 (33)	48 (27)	5 (3)
Chronic drinking problem	9 (5)	35 (20)	57 (33)	66 (38)	8 (5)
Disturbed behaviour	6 (3)	43 (25)	60 (35)	59 (34)	5 (3)
Emotional care of dying patients	16 (10)	49 (23)	42 (26)	59 (37)	5 (4)

Assessment

Oxford doctors believe that psychological and social factors should be routinely assessed and recorded for inpatients, but many felt that this is unnecessary for out-patients. One-third (35%) said that when psychological factors appear to be an important cause of the presenting problems, they confine themselves to physical assessment; 40% did not feel they should concern themselves with the emotional care of regular attenders with chronic physical illnesses.

Treatment

Most agreed that hospital doctors should be able to use simple psychological methods such as listening, reassurance, discussion of anxieties and problems, and discussion with relatives. Less than one-quarter ever use behavioural methods, and only 55% regularly see relatives.

Eighty one per cent said that the hospital doctor ought to be able to use psychotropic drugs: 43% use antidepressants, the most popular being amitriptyline and mianserin, but the dosages listed were often low compared with psychiatric practice and the recommendations of the British National Formulary. Benzodiazepines are widely prescribed, mainly as hypnotics and anxiolytics, but also as anticonvulsants, muscle relaxants, and for premedication. Treatment of acute organic states was very variable, and many doctors described inadequate dosages and inflexible regimes: chlormethiazole was the most popular drug, especially for alcohol withdrawal and commonly as a hypnotic in the elderly. Phenothiazines were used by 53%, most commonly as antiemetics, but haloperidol was little used (16%).

Help from others

Most Oxford doctors would like more help in providing psychological and social care, but this was not so for the minority, who felt that hospital doctors are not responsible for emotional care ($P<0.05$); 61% would like more help from non-medical staff and 60% better educational aids.

Just over half wanted more contact with the psychiatric service, but 24% felt that psychiatrists had little to offer in a general hospital. The main reasons given for referral to psychiatrists were diagnostic problems, depression, and disturbed behaviour. Few doctors felt that acute organic states, dementia, and non-compliance should be referred. The commonest reasons for not referring were similar to those reported by Mezey & Kellett (1971): the belief that patients dislike referral (75%), the disadvantages of being regarded as a psychiatric case (57%), and the ineffectiveness of psychiatric treatment (45%).

TABLE II

Comparison of physicians' and surgeons' replies (%) All figures are significantly different ($P<0.05$)

	Surgeons	*Physicians*
Emotional problems are part of the hospital doctor's work	73	90
Psychological factors are important in the course of physical illness	67	85
The variety of emotional and social care enhances interest	60	85
Emotional care is impractical under present conditions	44	18
I would welcome more non-medical help	52	73
General practitioners are responsible for assessment of emotional problems in new out-patients	76	35
Management of emotional problems is an important part of my care of chronic out-patients	47	99
The management of my patients' emotional problems is mainly the responsibility of nursing staff	49	22
Hospital doctors should be able to use psychotropic drugs	72	92
I frequently discuss problems with relatives	37	76
I use antidepressants frequently or occasionally	22	67
I would welcome more contact with psychiatrists	43	68

- Although satisfied with our psychiatric consultation service, many doctors wanted greater personal contact with senior psychiatrists: 29% said they were dissatisfied with this aspect and only 30% were completely satisfied. A number commented that they would like to know more about what psychiatrists have to offer in the management of medical and surgical patients, and several replies suggested joint meetings.

The pattern of replies

Answers to our questionnaire varied widely, even amongst doctors with similar jobs. We examined three possible explanations: the type of patient seen, specialty and seniority.

Type of patient. Doctors who treat patients with chronic disabling illness were much more likely than those who provide acute care ($P<0.05$) to see themselves as having an important responsibility for emotional care. They were also more likely ($P<0.05$) to report that they routinely assess their patients' mental state, discuss problems on ward rounds, see relatives, and use antidepressants.

Specialty. There were differences between physicians' and surgeons' replies to the majority of our questions (See Table II). Although there were striking individual exceptions, the surgeons were significantly less interested in emotional problems and felt less responsibility for them ($P<0.05$). They said that psychological and social care is impractical at present, and were less likely than physicians to want more help from psychiatrists or non-medical staff ($P<0.05$). In contrast, most physicians believe psychological care is important, say they would like to do more themselves, and are much more likely to see it as a medical rather than nursing responsibility ($P<0.05$).

Geriatricians, and to a lesser extent those working in medical specialities concerned with chronic disorders, stood out in their emphasis on all aspects of psychological care. General and specialist surgeons were the least interested groups, reporting that their patients had little need for pyschiatric or any other extra help, though accident and orthopaedic surgeons were concerned about the difficulties of treating the elderly confused: they discuss emotional difficulties on ward rounds, obtain more information about home circumstances, and want more psychiatric help. Obstetricians and gynaecologists were the only surgical group to say that psychogenic problems are common in their clinics. Most said thay assess the mental state of out-patients, discuss their problems, and would like more help from both psychiatrists and nurses.

Seniority. Consultants see psychiatric referral as less useful than do their juniors ($P<0.05$), but were more likely ($P<0.05$) to agree that emotional care is part of the hospital doctor's work and that it enhances its interest. The pattern of replies and comments suggests that the juniors are interested, but because they are so busy providing acute medical care, they see emotional and social problems as a nursing responsibility.

Discussion

Much has been written about the very small proportion of general hospital patients who are referred for a psychiatric opinion, but this paper describes the first detailed study of hospital doctors' attitudes to psychological and social care of their patients' difficulties. We have reported what Oxford doctors *say they do* rather than what they *actually do*, and it may be that our figures over-estimate their interest in psychological care. Even so, there can be no doubt that although hospital doctors believe psycho-social care is important they have widely differing views about what can and should be provided. This can mean that within a single unit, one doctor sees that psychological and social care as an important part of his everyday work, while a colleague with an identical job sees little value in assessment, treatment, or referral.

We have already emphasised that there can be no right or wrong answers to our questions. Although both hospital doctors and psychiatristis believe that emotional care of general hospital patients is important, it is uncertain what forms of help are most needed and who should be providing them. Needs vary with the type of clinical unit, and psychological and social care are often best provided by other members of the team or by the general practitioner. However, hospital doctors do have overall clinical responsibility for in-patients and for some out-patients, and we need to be explicit about the knowledge and skills they require. There is an obvious need for further research, including both improved questionnaires and observation of clinical practice, in this it should be possible to use methods and ideas already well-established in general practice (Goldberg & Huxley, 1980). Such research should include the need for psychological treatments in the general hospital, the extent to which these can be provided by the doctors and nurses of the clinical teams, and the way in which psychiatrists can best help.

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*Richard Mayou, FRCP, FRCPysch, *Clinical Reader in Psychiatry, University Department of Psychiatry, Warneford Hospital, Oxford OX3 7JX*

E. B. O. Smith, FRCP (Edin), FRCPsych, *Consultant Psychiatrist, John Radcliffe Hospital, Oxford*

*Correspondence

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A HUNDRED YEARS AGO

"*Crighton Royal Institution*—The number of pauper patients has been kept down by the discharge of all who were fit to reside out of the asylum, and most of those discharged unrecovered were boarded out in private dwellings. This policy has been steadily pursued for the last few years, with the result that the number of pauper patients belonging to the district has fallen from 302 to 239."

Reference

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Conversion Without Hysteria: A Case Report and Review of the Literature

ARIEH SHALEV and HANAN MUNITZ

The term 'conversion' implies a correlation between conversion symptoms, hysteria, and hysterical personality. A clinical case of conversion related to chronic post-traumatic disorder, with paranoid features, was successfully treated by anti-psychotic drugs; it illustrates the non-specific nature of conversion symptoms. Mechanic's concept of 'illness behaviour' is a frame-work that meets the need for a broader understanding of conversion symptoms.

'Conversion' and 'Hysteria' are controversial terms; Slater (1969) even denied their right to be considered as independent diagnostic categories. In its broader definition, 'Hysteria, Conversion type' is a "Psychogenic disturbance of some part of the body" (World Health Organisation, ICD9, 1978). This definition includes three basic assumptions: a psychological interference with body functions, a wide variety of body functions involved, and a correlation of conversion with hysteria. A brief review of the contradictory positions concerning each of these three assumptions might help therefore, to clarify the actual controversy concerning the concept of conversion.

The mode of interference of pyschological factors with body function in conversion is unknown, but one of the traditional ideas is that psychological factors interfere in a way that conveys symbolic meaning to the symptoms. The presence of symbolic meaning is an essential feature of 'Conversion Disorder' in the DSM III (American Psychiatric Association, 1980; Nemiah, 1980). That same idea is widely criticised by others (Slater, 1965; Lazare, 1981; Trimble, 1981; Kendell, 1983), and is not included in the ICD9.

There are two positions about the symptoms involved. One follows Guze's (1971) definition of conversion as "Unexplained symptoms suggesting a neurological disease", and tends to separate conversion symptoms from other somatic expressions of psychological distress such as 'Somatization disorder' (Briquet syndrome), 'Psychogenic pain and Hypochondriasis' (DSM III, 1980). The other position admits a large overlap between Briquet syndrome and conversion reaction (Merskey, 1979) or includes symptoms that are not defined by neurological examination in the category of conversion (Kendell, 1983). Historically, the correlation between conversion and neurological dysfunction, as well as the idea of symbolic meaning, are part of the Freudian tradition, based on Charcot's demonstration of both the linkage and the contradiction between conversion and neurological disease (Freud, 1895).

As to the correlation of conversion and hysteria, it was Freud (1895) who named this clinical phenomenon, known for centuries, as Conversion—the proper name of a psychodynamic mechanism that he described in hysterical patients. This mechanism includes the repression of an unacceptable wish, followed by the transformation (conversion) of its energy component into somatic dysfunction, and was believed to be the typical defence mechanism of hysteria and, later on, of hysterical personality (Reich, 1949).

'Conversion' implies, therefore, the presence of the same psychodynamic mechanism behind the symptoms, and a correlation between the occurrence of conversion symptoms, hysteria, and hysterical personality.

These implications should be reconsidered and we present a clinical case report, demonstrating the difficulties related to the concept of conversion. We also discuss the presumed correlation of conversion symptoms to the psychodynamic mechanism of conversion and propose, after Mechanic (1968) and others, a new definition of conversion.

Case Report

Mr. A, a 72-year-old man, was born in Poland, is married, and has no children. In 1981, he was admitted to our closed psychiatric ward in a regional psychiatric hospital because of paranoid delusions, extreme self-neglect, and starvation. He had participated in World War II, and had been buried for 24 hours under the ruins of a building, after which he was discharged and officially recognised as a disabled veteran; He suffered from paralysis of his right arm. He worked occasionally as an unskilled labourer, his social life was reduced to a minimum, and he maintained only the most necessary contacts with social agencies. In 1960, when his disability was officially recognised, he stopped working, and lived on his pension; he and his wife immigrated to Israel in 1978. Three months before his admission, his wife had a stroke and was hospitalised, after which he was confined in his apartment, did not dare to go out, neglected himself, and was starving. A few days before admission, he attacked his neighbours, claiming that they were stealing from his post box. A home visit revealed marked neglect and signs of long-term paranoid organisation (e.g. the house entrances were marked by pieces of paper, so that any attempt to open them without leaving signs was impossible).

On admission, his sensorium was clear and he was well orientated, showing psychomotor excitement and persecutory delusions without hallucinations, a paralysis of his right arm was found, without musculuar atrophy and with normal and symmetrical reflexes. No wounds or scars were seen, despite Mr. A's insistence on the presence of such on his skin. The rest of the examination, biochemical studies, and E.E.G. were normal.

Besides his persecutory delusions, the paralysis and the injury that preceded them were the central issue of Mr. A's thoughts, though he could not remember a precise event in which he was injured. He was diagnosed as suffering from paranoid psychosis, probably on the basis of an old combat reaction, and from conversion paralysis of his right arm.

We started treatment with haloperidol, 15 mg a day. His psychomotor excitement, thought disorder, and delusions receded, in that order, over four weeks, and at the same time, his paralysis disappeared. There was no psychological elaboration of memories from the war, and no abreaction. No attempt was made to explore with him his past or to confront him with the fact that there were no signs of wounds on his skin. He was discharged showing significant improvement but, after a month, asked to be readmitted because he could not manage on his own. During two years' follow-up, neither psychosis nor conversion recurred.

Discussion

This case is characterised by the simultaneous occurrence of paranoid psychosis and conversion, and by the disappearance of both under antipsychotic pharmacotherapy. Although it can be argued that Mr. A's psycho-pathology is much older, and that he was suffering from post-traumatic disorder, the case is nevertheless one of a chronic conversion symptomatology, treated in a very unorthodox way. The question of the specificity of conversion symptoms refers to whether these symptoms, as psychoanalytical theory argues, correlated with specific life events which are meaningful for the individual, and raise unconscious and unresolved psychological conflicts, or whether they represent a variety of responses to stressful conditions, without a specific pathogenic agent and without a specific psychodynamic mechanism?

The literature, can be analysed by focussing on five issues:

A. The evolution of the psychoanalytical concept of conversion

The interpretation of conversion symptoms and the formulation of the underlying mechanism are the point of emergence of psychoanalytic discovery by Freud, and the cornerstone of psychoanalytical theory. It is from this that both the basic assumption of the existence of the unconscious and the basic concept of repression stem.

In the psychoanalytical conceptualisation of conversion, there is a clearly defined evolution: the mechanism by which conversion symptoms are formed is still believed to be the same, but the nature of the drive beyond conversion symptoms is nowadays differently understood.

The conversion mechanism includes a wish that is unacceptable to the individual and that has to be repressed; following this, the energy component of the drive is converted into a somatic symptom, and the representational part of the wish is kept out of awareness. The resulting symptom: *cathects* the energy of the drive, and thereby protects the individual from undesired affects; *expresses* symbolically the incompatible wish; allows the individual to avoid confronting conflicting parts of himself (*primary gain*); and can later on constitute a way to escape from painful situations (*secondary gain*).

The understanding of this mechanism has not changed since Freud; in psychodynamic terms, the basic therapeutic goal, remains the undoing of repression, which results in an affective catharsis (*abreaction*), followed by resolution of the symptom.

There are many new ideas about the nature of the *Drive*. Freud assumed that in hysterical conversion, repression is basically used against sexual drives but more recent authors include other conflicts (Fenichel, 1945; Rangell, 1959), and argue that conversion should be separated from hysteria (Sperling, 1960) and from hysterical personality. Kernberg (1975) attributes conversion symptoms that are multiple, elaborate, or bizarre to the borderline personality, where they involve aggressive drives, and are related to very early conflicts.

Much information concerning psychogenic

conversion reactions has been accumulated by military psychiatry; they are often encountered in combat reactions, where the conflict is assumed to be one between self-preservation and task accomplishment (Shalev & Tyano, 1981). The correlation of conversion symptoms and survival in battle conditions and their quick remission when the threat vanishes were already noted by Kretschmer (1961) in World War I.

Thus, the psychoanalytical approach does not correlate the occurrence of conversion to a specific conflict or a particular type of personality, but still conserves the basic mechanism described by Freud.

B. The incidence of conversion

Ljunberg (1959) estimates that the incidence of conversion in the general population of Sweden is 0.5%; similar results (0.4%) were obtained in a United States urban community by Weissman *et al* (1978).

Guze *et al* (1971) found that among 500 psychiatric out-patients, 24% had a history of at least one conversion symptom, and 10% had more than one.

It is of much interest that similar results were obtained by Farley *et al* (1968) in 100 women evaluated after a normal pregnancy (27%); by Woodruff (1967) in 50 medically ill women (30%), and by Engel (1970) in patients admitted to a general medical service (24%). Trimble (1981) compared the incidence of the diagnosis of hysteria at the National Hospital, Queen Square in three different periods (1951, 3,5; 1961, 3,5 and 1971, 3,5), and found that the decline in this diagnostic category from the fifties (1.55%) to the sixties (0.85%) did not continue into the seventies and that its incidence remains around 1%.

From all these reports, it seems that this type of symptom is quite frequently diagnosed, has a very high life prevalence, and is not specific to psychiatric populations.

C. Conversion and personality

Table I shows the results of the principal reports concerned with the correlation between conversion symptoms and personality structure. The prevalence of hysterical personality in people suffering from conversion symptoms was evaluated by Ljunberg (1957), Chodoff & Lyons (1958), Slater & Glithero (1965), and Merskey & Trimble (1979). All these authors obtained similar results: 17–20%.

Concerning other types of personality Merskey & Trimble (1979) reported that their sample of 89 patients with conversion included 17 with hysterical personality (19%), 17 with passive immature dependent personality (19%), seven with obsessional personality (8%), and 16 without pathology (18%). Guze *et al* (1971) note that conversion is significantly more often associated with hysteria, with antisocial personality, and with affective disorder. It can be concluded that most of the time, conversion symptoms do not occur, in patients with hysterical personality or hysterical neurosis, but that they do appear in many other types of personality and disorders.

D. Conversion and somatic diseases

Research in this field emphasises the correlation between conversion and somatic diseases, especially neurological ones.

Tiessenbaum *et al.* (1951) found that 13% of 395 neurological patients are diagnosed in an earlier stage of their illness as suffering from "functional" symptoms, i.e. conversion, while conversely McKegney (1967) found coexisting organic disease in 47% of 144 patients with conversion symptoms referred for psychiatric consultation from medical and surgical wards. Merskey & Buhrich (1975) reported that 43 out of 89 conversion patients (Table II) suffered from an organic brain syndrome or systemic disease affecting the brain: the frequent association of epilepsy and conversion (23 cases: 26%) is a remarkable finding here. Whitlock (1967) compared the prevalence of somatic disease in conversion patients and in a control group, finding a much higher prevalence in the first (63% *versus* 5%).

TABLE I
Conversion and personality: review of findings

1. *Prevalence of hysterical personality*		
Chodoff & Lyons (1958)	$n = 17$	17.6%
Ljunberg (1957)	$n = 381$	21%
Slater (1965)	$n = 85$	21%
Merskey (1975)	$n = 89$	19%
2. *Other types of personality*		
Merskey & Trimble (1979)	Hysterical	19%
	Immature	19%
	Obsessive	8%
	Others	36%
	Normal	18%
Guze (1971) "conversion significantly more frequently associated with"		
	Hysteria	
	Antisocial affected disease	

TABLE II

Conversion and somatic disease

McKegney (1967)		$n = 144$		47%
Merskey & Buhrich (1975)		$n = 89$	23 with epilepsy 4 with cardiovascular disease 4 with multiple sclerosis 4 with head injury 4 with dementia 4 with encephalitis	
				Total 48%
Slater & Glithero (1965)	(1965)	$n = 85$	19 subj. C.N.S. disease (22 with C.N.S. disease on follow-up)	
				Total 48%

TABLE III

General prognosis of conversion

	n	*Follow up (years)*	*Results*	
1. *Good prognosis studies*				
Carter (1949)	100	4–6	Well or improved	86%
Ljunberg (1957)	381	1	Improved	62%
		5	Improved	77%
		15	Improved	80%
Hafiez (1980)	61	1	Without relapse	80%
2. *Bad prognosis studies*				
Slater (1965)	85	7–11	Severely disturbed	85%
Gatfield & Guze (1962)	24	2.5–10	Still sick	88%
Guze & Perley (1963)	29	3–10	Sick at follow-up	85%
Lewis (1975)	98	7–12	Disabled	45%

One of the most important studies is that of Slater & Glithero's (1965). They followed up a group of 85 patients, diagnosed initially as conversion hysterics, for seven to 11 years, and found that 19 were initially suffering from combined organic pathology and conversion, 22 others developed neurological illness during follow-up, and 12 others died—four from suicide. In more than half the series, conversion was associated with organic pathology.

According to these results, conversion is very often associated organic pahology; in many cases, an initial diagnosis of conversion is changed to one of organic illness and, in others it coexists with organic pathology.

E. The prognosis of conversion

Follow-up is an important source of information concerning the nature of a clinical phenomenon, and it reveals that conversion can remit or develop into either organic or psychiatric disorder. In many patients, an organic disease is found, (e.g. 30% of previously undiagnosed neurological pathology in the sample of Slater & Glithero). In 2.5 to ten years' follow-up of patients discharged from a neurological ward with the diagnosis of conversion, Gatfield & Guze (1962) found that 21% developed a well-defined neurological disease. Raskin *et al* (1966) followed-up 50 conversion patients, and found that in 20%, an organic pathology appeared during the first year of follow-up. Finally, Stefansson *et al* (1976) found a neurological disease in 13% of conversion patients, in 3.3 years of follow-up.

The general prognosis of conversion is a matter of controversy (Table III), some authors reporting a relatively good outcome (Carter, 1949; Ljunberg, 1957; Hafiez, 1980) and others a much poorer one (Slater & Glithero, 1965; Gatfield & Guze, 1962; Guze & Perley, 1963; Lewis, 1975). These differences are probably due to the different populations involved, patients recruited from psychiatric consultation doing better than those released from neurological wards.

Discussion

The review of the literature shows that conversion is a fairly frequent symptom which is not specific to hysteria; it appears in a wide variety of personalities, in stressful situations such as combat reaction, and in various psychotic and neurotic conditions. Its symptoms also occur as precursors of schizophrenia or in association with depressive illness. Conversion is often associated with pathology in the nervous system and especially with epilepsy; it is often a premonitory sign of evolving somatic disease. The psychoanalytical literature presents a similar trend towards a broader distribution of conversion symptoms among various pathologies.

It seems, therefore, that conversion should be considered as a variety of response to non-specific sources of distress or threats to homeostasis. We therefore propose, by analogy to the term 'hysteria', which was a misnomer based on a concept of the wandering womb as source of pathology, that 'conversion' should be dissociated from the psychodynamic mechanism which gave it its name.

Paradoxically, the non-specificity of conversion symptoms is a well documented subject, which seems to be overlooked by many modern textbooks. Slater (1965), Slater & Roth (1969) and more recent British sources (Sutherland, 1973; Trimble, 1981; Gelder *et al.*, 1983; Kendell, 1983) have been reluctant to consider conversion as specifically related to hysteria, but they conserve the "tough old word hysteria" which "will tend to outlive its obituarists" (Lewis, 1975) as a framework for classifying conversion reactions. Gelder *et al* (1983) argue that "hysterical symptoms are very common, hysterical neurosis is not", illustrating this same position.

In other textbooks (Abse, 1974; Stein, 1977; Nemiah, 1980), conversion is discussed in a very specific relationship to hysteria. In particular, it is only rarely mentioned as premonitory sign of psychotic conditions, affective illness, or organic diseases (Berger, 1980).

The terms 'neurosis' and 'hysteria' have been banished from the official classification of the American Psychiatric Association, but the presence of symbolic meaning is, nevertheless, considered an essential feature of the new 'Conversion disorder' in DSM III.

In his discussion of hysteria, Kendell (1983) denotes the need for a new and comprehensive concept to account for the vast array of pathologies encountered under this heading. The concept advanced both by him and by Trimble (1981) and Ludwig (1980) is Mechanic's (1968) concept of 'Sick role and illness behaviour'. Illness behaviour (Mayou, 1984) is the end-result of three categories of factors that accompany human illness: the fact of physical disease, the emotional reaction to threat (real or imaginary), and the pattern of reaction that results from learning and habituation of the individual to socially acceptable ways of escape from undesired situations. "Most illness behaviour is generated by recognised disease... but substantial parts of the whole are generated either by the fear of disease, or by 'positive reinforcement' provided by the advantages of the invalid role" (Kendell, 1983).

A redefinition of conversion as *a mode of reaction to illness* seems particularly adequate, because it includes all the various conditions with which conversion reaction can be associated. Pilowsky (1977) defined a group of clinical manifestations as 'abnormal illness behaviour', and conversion hysteria was included in this category by Trimble and by Ludwig. However, in regard to human behaviour under threat, abnormality is a matter of judgement, and overlooks the adaptive value that conversion might have (Kretschmer, 1961).

We suggest, therefore, that conversion should be defined as "a variety of illness behaviours, characterised by unexplained symptoms, suggesting a neurological disease, occurring in a wide variety of medical and psychological disorders". This redefinition has an important clinical value: it encourages the clinician to focus his intervention on the actual source of distress, instead of looking for the hidden significance of symptoms. The case report presented above is an example of this approach.

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*Arieh Shalev, MD, *Senior Psychiatrist, Gehah Psychiatric Hospital, Beilinson Medical Centre, Petah Tiqva and Tel Aviv University Sackler School of Medicine, Tel Aviv, Israel*

Hanan Munitz, MB, BS, *Head of Department A, Gehah Psychiatric Hospital, and Head, Department of Psychiatry, Tel Aviv University Sackler School of Medicine*

*Correspondence to Gehah Psychiatric Hospital, Beilinson Medical Centre, Petah Tiqva 49 100, Israel

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Effects of Intravenous and Subcutaneous Administration of Apomorphine on the Clinical Symptoms of Chronic Schizophrenics

E. K. G. SYVÄLAHTI, E. SÅKÖ, M, SCHEININ, K. PIHLAJAMÄKI and J. HIETALA

The effects of apomorphine, a stimulant of dopamine autoreceptors, were studied in 12 chronic schizophrenics on neuroleptic treatment; both subcutaneous and intravenous administration were used. Apomorphine has been reported to have therapeutic effects in previous studies but, we were not able to confirm any significant and specific differences in psychotic symptoms or tardive dyskinesia scores with apomorphine administration, compared with placebo. These results do not support the importance of dopamine autoreceptors in the regulation of schizophrenic and dyskinetic symptoms in chronic neuroleptic-treated patients.

A large body of both clinical and pre-clinical research has fostered hypotheses that the neurotransmitter dopamine (DA) is of major importance in the biochemical study of schizophrenia. Theories on the existence of multiple dopamine receptors in man (Carlsson, 1975; di Chiara *et al*, 1978; Meltzer, 1979) are of considerable clinical importance, since new types of drugs and treatment strategies are needed to help those schizophrenic patients who do not respond to standard neuroleptics. Recently, special attention has been focused on DA autoreceptors found in the pre-synaptic terminals of the dopamine neurons (Carlsson, 1975; Meltzer, 1979). One experimental tool for studying these receptors is apomorphine, a direct but partial DA agonist, which stimulates DA autoreceptors when administered in small doses (see Meltzer, 1982). It has been suggested that the apomorphine-induced reduction in dopaminergic activity is responsible for the putative anti-psychotic effects (Corsini *et al*, 1977; Smith *et al*, 1977; Tamminga *et al*, 1978; Di Chiara *et al*, 1978; Cutler *et al*, 1982). However, schizophrenics form a most heterogenous and unstable group of patients, and spontaneous and/or placebo-related changes may occur in schizophrenic symptoms. On the other hand, apomorphine has non-specific sedative properties which may calm excited and confused patients (Feldman *et al*, 1975; Corsini *et al*, 1977). Another factor is that the dose and route of administration of the drug may influence the results.

In a recent study (Ferrier *et al*, 1984), no specific therapeutic effect in unmedicated acute or chronic schizophrenics could be demonstrated for subcutaneous apomorphine (other than a reduction in anxiety in acute cases). DA autoreceptors may become supersensitive following chronic neuroleptic treatment (Nowycky & Roth, 1977; Bannon *et al*, 1982), and this might have impact on the effects of DA autoreceptor agonists. We report here the effects of subcutaneous injection and intravenous infusion of apomorphine, and corresponding placebo administrations, in schizophrenics under neuroleptic treatment.

Methods

Subjects

Twelve male in-patients (mean age 30·6 years, range 28 to 39 years) gave informed consent for the study which was ethically approved; all were in good physical condition and were normotensive. The diagnosis according to the DSM-III, duration of illness (time from the first contact with a doctor because of schizophrenic-like symptoms), neuroleptic treatment, and drugs used are shown in Table I. The medication was kept stable for at least four weeks, before and throughout the study periods; only one patient had anticholinergic treatment. One patient withdrew after the first (placebo) injection because of excess anxiety.

At weekly intervals, a subcutaneous injection of either 0.005 mg/kg apomorphine or identical vehicle was given to eight patients, in randomised order and under double-blind conditions. Five months later, apomorphine (0.015 mg/kg/90 minutes) or physiological saline was infused into a dominant forearm vein of seven patients. This was done blindly, using a Braun Perfusor^R ED 2 pump, with an interval of one week between placebo and apomorphine infusions. Our pilot experiments in healthy volunteers showed that an infusion of 0.015 mg/kg in 90 minutes was well tolerated and gave reproducible responses in neuroendocrine challenge tests. The experiments started at 8 a.m. and the drugs were administered after a minimum rest period of 30 minutes. The patients

TABLE I

DSM–III diagnosis, age and duration of illness and neuroleptic treatment of the patients (drug treatment was maintained stable at least four weeks before and throughout the study period)

Patient	*Diagnosis (DSM III)*	*Age (years)*	*Duration of illness (years)*	*Neuroleptic treatment (years)*	*Current treatment (mg/day)*
1	295.12	31	12	12	Perphenazine (24) Chlorpromazine (100)
2	295.34	29	8	8	Chlorpromazine (800)
3	295.14	28	6	6	Chlorpromazine (400)
4	295.14	28	8	86	Chlorpromazine (300)
5	295.22	34	6	6	Perphenazine (12) Levomepromazine (50)
6	295.12	31	12	12	Thioridazine (600) Biperiden (2)
7	295.92	27	6	6	Clopenthixol (50) Levomepromazine (100)
8	295.02	33	7	7	Chlorpromazine (200)
9	295.92	39	14	12	Flupenthixol (3) Lorazepam (2)
10	295.12	28	4	4	Thioridazine (150)
11	295.14	27	7	7	Chlorpromazine (150) Penfluridol (40) (per week)
12	295.24	32	7	7	Chlorpromazine (400)

TABLE II

BPRS total scores before cutaneous injections (0.005 mg/kg) and intravenous infusions (0.015 mg/kg/90 min) of apomorphine and placebo, and at 60 minutes after administration of the drugs

	Injection				*Infusion*			
	Apomorphine		*Placebo*		*Apomorphine*		*Placebo*	
	pre	*post*	*pre*	*post*	*pre*	*post*	*pre*	*post*
Pat 2	49	45	53	54	67	69	65	68
3	49	53	76	65	—	—	—	—
4	75	65	68	75	55	48	52	38
5	54	59	67	70	—	—	—	—
6	51	56	43	39	—	—	—	—
7	51	51	41	35	60	60	59	59
8	36	31	39	36	39	40	42	32
9	41	31	47	47	—	—	—	—
10	—	—	—	—	28	28	29	23
11	—	—	—	—	48	47	49	56
12	—	—	—	—	53	51	56	53
mean	50.75	48.88	54.25	52.63	50.00	49.00	50.29	47.00
SEM	4.05	4.41	5.02	5.61	4.96	5.00	4.50	6.14

maintained a recumbent position throughout. Blood samples for hormone and plasma HVA analyses were withdrawn from cannula in the non-dominant forearm several times before, and during, a period of 210 minutes from the administration of the drugs. The biochemical samples are being analysed and these results will be presented separately.

Psychiatric assessment was made by a psychiatrist (E.K.G.S.) at 0, 30, 60, and 120 minutes using the Brief Psychiatric Rating Scale (BPRS) (Overall & Gorham, 1962). The rater did not know whether an active drug or placebo was administered. The BPRS items were grouped in five factors or syndromes: anxiety-depression, anergia, thought disturbance, activation, and hostile suspiciousness, according to Guy (1976).

Disturbances in the extrapyramidal system were assessed, also blindly, by a neurologist (ES) at 0, 60, and 120 minutes, using a rating scale for tardive dyskinesia and related neurological side-effects (Gerlach, 1979). The scores were assessed both while the patient was unoccupied and undisturbed and while he was active and performing voluntary hand movements or drawing.

Results

There was only a slight and statistically insignificant decline in the total BPRS scores at 60 minutes after subcutaneous injection of apomorphine (from 50.8 ± 4.1 (SEM) to 48.9 ± 4.4) ($n = 8$) (Table II). After placebo injection, the corresponding reduction was from 54.3 ± 5.0 to 52.6 ± 5.8. There were no significant differences between the effects of apomorphine and placebo at any time during the study, as measured by the total BPRS scores. Four patients showed a slightly greater decrease in the BPRS total scores after apomorphine than after placebo, but four responded better to placebo.

After the intravenous infusion of apomorphine, the decline of BPRS total scores from the pre-treatment values of 50.5 ± 5.0 to 49.0 ± 5.0 at 60 minutes was comparable to mean scores during placebo infusion (from 50.3 ± 4.5 to 47.0 ± 6.1) ($n = 7$). Two patients showed a slightly better response to apomorphine than to placebo infusion, and four had a greater fall in total BPRS scores after placebo than after apomorphine. The changes in BPRS scores were, however, generally rather small, and no striking alterations in the clinical symptomatology could be observed.

No systematic drug-related changes could be documented in any of the five factors of the BPRS; the individual changes varied between one and three points in most cases. The occasional changes that did occur could not be associated with any particular patient or disease form, and corresponding small changes took place, also, after placebo.

The slight changes in the scores for general dyskinesia after apomorphine injection (from 19.9 ± 3.2 to 17.9 ± 2.1) ($n = 8$) and infusion (from 11.1 ± 2.7 to 11.3 ± 2.6) ($n = 7$) were not statistically significant. After placebo infusion, a slight but statistically significant decrease from 16.6 ± 2.7 to 11.7 ± 2.5 was seen ($P < 0.05$, matched pair t-test). Thus, spontaneous changes in tardive dyskinesia symptoms can be seen during rest. The only patient taking anticholinergics showed a decrease in dyskinesia scores (from 22 to 13) after apomorphine injection, but not after placebo. Changes in dyskinesia in individual patients were not related to the changes seen in the BPRS scores. No significant changes in the clinical symptoms of Parkinsonism were seen after apomorphine or placebo treatment.

Side-effects were mild and of short duration. One patient reported increased anxiety 10–30 minutes after the apomorphine injection, and one complained of dryness of the mouth 30 minutes after apomorphine injection. After placebo, one patient complained of nausea and dizziness, while another reported nausea at ten minutes and headache at 90 minutes.

Discussion

The potential clinical usefulness of DA autoreceptor stimulation in clinical psychiatry is mainly based on the notion that increased dopaminergic activity is important in psychosis and in tardive dyskinesia. The results of the present placebo-controlled study indicate, however, that low doses of a DA agonist, apomorphine, do not induce any clear therapeutic change in chronic schizophrenics on neuroleptic treatment. This is in accordance with the recent findings of Ferrier *et al*, (1984), of no significant improvement in psychotic symptoms in unmedicated acute or chronic schizophrenics after 0.75 mg apomorphine given subcutaneously. Previously, apomorphine has been reported to provide rapid, although transient improvement of psychotic symptoms in a sub-population of medicated (Tamminga *et al*, 1978; Cutler *et al*, 1982) and unmedicated (Corsini *et al*, 1977; Smith *et al*, 1977; Di Chiara *et al*, 1978) schizophrenics.

On the other hand, chronic treatment with bromocriptine, or other ergot alkaloids with DA agonist activity, has not been clinically beneficial in patients receiving neuroleptics (Tamminga & Schaffer, 1979; Beaumont *et al*, 1975), but a slight improvement was noted in some unmedicated chronic schizophrenics (Meltzer *et al*, 1983). Thus, the responses of schizophrenic patients to apomorphine and other DA agonists seem to vary in different patients and studies, and the role of presynaptic DA receptors in schizophrenia still remains unclear. In any case, the original enthusiasm about the therapeutic potential of apomorphine in schizophrenia should be diminished.

Animal (Nowycky & Roths, 1977) and clinical data (Cutler *et al*, 1982) suggest that the activity of pre-synaptic dopamine receptors in the central nervous system may be altered by chronic treatment with neuroleptics, and that supersensitivity of the pre-synaptic receptor may take place (Bannon *et al*, 19820). Tamminga & Schaffer, (1979) reported that apomorphine (3 mg s.c.) produced improvement in nine out of 18 chronic schizophrenics treated with neuroleptics, while Cutler *et al* (1982) found improvement in the BPRS in two out of five neuroleptic-treated chronic schizophrenics after the same dose of apomorphine (0.005 mg/kg s.c.) as used in the present study. However, Hollister (1981) found no benefit from the addition of either high or low doses of apomorphine to neuroleptics in the treatment of schizophrenia. The results of the present study indicate that utilising autoreceptor agonists as complementary therapy to neuroleptics does not lead to increased therapeutic effects.

Only relatively small series of patients can be studied with the present methodology; the possibility cannot be excluded that minor sub-groups of neuroleptic-treated patients may exist who might respond to DA autoreceptor agonists. Di Chiara *et al* (1978) reported decreases in psychotic symptoms in paranoid and hebephrenic (disorganised), but not catatonic patients after 1 mg apomorphine i.m. Corsini *et al* (1977) reported that apomorphine was most effective in schizo-affective manic patients, but had little effect in chronic schizophrenia. Our study consisted of several types of chronic schizophrenic patients (six disorganised, two catatonic, two undifferentiated, one paranoid and one patient with a residual illness. However, none of the patients showed clear apomorphine-related changes in their psychotic symptoms. Thus, the different clinical manifestations of the illness do not seem to differ markedly in their response to apomorphine administration. The results of Cutler *et al* (1982) suggest that a consistent anti-psychotic effect does not necessarily follow a consistent alteration in DA metabolism, and this might in part explain the negative findings. It is possible that a supersensitivity is seen only in a minor, biochemically, but not necessarily clinically, distinct patient group; or only during certain acute episodes of the illness; or, it is perhaps only manifest after withdrawal of neuroleptic drugs.

In accordance with our findings, Jeste *et al* (1983) recently reported that there were no significant changes in psychopathology with apormophine (0.005–0.04 mg/kg s.c.) or placebo, as judged by changes in the total BPRS score in their sample of 12 schizophrenic patients. They found, however, a significant alleviation of depression and anxiety after apomorphine. A reduction in acute schizophrenics' anxiety ratings after apomorphine was the only significant therapeutic effect in the study by Ferrier *et al* (1984), too. We cannot directly confirm these findings, and the sedative properties of apomorphine (Feldman *et al*, 1975; Corsini *et al*, 1977) may induce non-specific effects. One patient responded slightly better to apomorphine than to placebo in the present study, and the improvement was most clear in factor three (anxiety depression) of the BPRS. However, another patient showed a corresponding change in the course of placebo infusion. This again highlights the difficulties involved in interpreting symptoms in schizophrenic patients under experimental conditions.

Apomorphine in doses between 1–6 mg s.c. has reduced the sensitivity of tardive dyskinesia in some (Carroll *et al*, 1977; Tarsy *et al*, 1979; Tolosa, 1978), but not in all studies (Meltzer, 1982). The effects have also varied greatly from one patient to another (Smith *et al*, 1977). The pathophysiology of tardive dyskinesia is still far from clear, and, like schizophrenia, is probably of diverse aetiology (Klawans *et al*, 1980). The results of the present study suggest that in most schizophrenic patients with dyskinetic symptoms, stimulation of DA autoreceptors by low doses of apomorphine does not induce clear changes in clinical symptoms; a subgroup of patients may exist who respond to apomorphine or other DA autoreceptor stimulants. With the development of more potent and selective receptor stimulants, more reliable answers can eventually be expected.

Acknowledgement

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*E. K. G. Syvälahti, MD. *(Acting) Professor of Pharmacology*

E. Säkö, MD, *Researcher in the Finnish Academy*

M. Scheinin, MD, *Researcher in the Finnish Academy*

K. Pihlajamäki, MD, *(Acting) Assistant Professor of Pharmacology*

J. Hietala, MB, *Research Fellow in Pharmacology*

Departments of Pharmacology, Psychiatry and Neurology, University of Turku, Turku 52, Finland

*Correspondence

(*Accepted 20 December 1984*)

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49, XXXXY Chromosome Anomaly: An Unusual Variant of Klinefelter's Syndrome

T. HARI SINGH and SUDHIR RAJKOWA

A case of 49, chromosome anomaly in an adult male of unusually large build, signs suggestive of Parkinsonism and mild episodic depression is reported.

History and clinical feature

A male, aged 34 is reported (adult case report—Tenbrink *et al*, 1976). His developmental milestones were delayed. At the age of 15 years he was noted to be "overgrowing". He suffers from a moderate to severe degree of mental handicap and is capable of simple repetitive tasks and packaging jobs in the Adult Training Centre.

He was admitted for long stay hospital care on the death of his mother when he was aged 33, having previously lived at home. He is one of three sibs, his brother and sister being of normal mentality.

On physical examination he is 6ft 6ins in height with a chest circumference of 45 ins. He weighs 294 lb. He has a pronounced dorsal kyphoscoliosis. He has a "mongoloid" facies with wide-spaced eyes and palpebral fissures that slant markedly upwards and outwards. He has a high-arched palate, bilateral cubitus valgus, and incurving fifth fingers and fifth toes. The bridge of the nose is depressed. The speech is nasal. The lower lip is very prominent and the chin is broad, giving the face a round configuration.

The chest is small with depressed sternum and widely-spaced nipples (Hayek *et al*, 1971). He has bilateral genu valgus and flat feet. He has no facial or pubic hair. The penis is rudimentary. The testes are descended but they are small and the scrotal development is poor. There is girdle obesity. He walks with a festinate gait and tends to fall forwards especially if carrying a weighty object. He has a course tremor of both hands. He dribbles excessively.

He is generally pleasant and cheerful, but has periods of withdrawal and irritability for no obvious reason. These episodes are short and have not so far required any treatment. He is stubborn and single-minded, which has resulted in occasional behaviour problems. He can feed himself, but needs assistance in dressing and bathing. He is toilet trained and shows interest in social activities. Serum testosterone level was very low, being 0.9 N mol/L (normal values between 10–30 N mol/L).

X-ray of the skull showed marked degree of microcephaly with quite marked thickening of the calvarium. On X-ray both elbows showed gross re-modelling of the lower end of the humerus and both the olecranon and radial head bilaterally. There was re-modelling of the rib cage and a congenital anomaly of the third and fourth dorsal vertebrae due to an infused hemi-vertebra, both components being present, giving rise to a scoliosis.

The EEG was suggestive of diffuse changes at both cortical and sub-cortical levels with low amplitude theta and delta frequency frequently interrupted by synchronous discharges of low to moderate amplitude.

Comments

Since the first description (Fracarro *et al*, 1960) of a patient with 49, chromosome anomaly, about one hundred cases have been reported in the world literature. The three main features of this syndrome (Hecht, 1982; Lewis *et al*, 1964) are mental handicap, usually of severe degree; hypoplastic male genitalia, and proximal radio-ulnar synostosis (Scherz & Roeckel, 1963).

These three features are present in the case described together with other characteristics not hitherto reported in connection with this karyotype. These include microcephaly, slanting palpebal fissures and other facial characteristics, vertebral anomalies, extreme tallness and large build, mild signs of Parkinsonism, and symptoms of mild depression and anxiety.

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*T. Hari Singh, MBBS, MRCPsych, *Consultant Psychiatrist, Llwyneryr Hospital, Morriston, Swansea and Hensol Hospital, Pontyclun, Mid-Glamorgan.*

Sudhir Rajkowa, MBBS, DTCD, MRCPsych. *Registrar in Psychiatry, Cefn Coed Hospital, Swansea. (Present appointment: Senior Registrar, Child and Adolescent Psychiatry, Child and Family Guidance Service, Collegiate House, College Street, Leicester*

*Correspondence

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49, XXXYY Chromosome Anomaly in a Mentally Retarded Man

VALERIE A. COWIE, K. RAMESHWARI SINGH and RICHARD WHEATER

A case of 49, XXXYY chromosome anomaly in an adult male is reported. Features of Klinefelter's syndrome are predominant among the clinical findings. Characteristics suggestive of acromegaly have been associated with this chromosomal anomaly. Despite prognathism and an overhanging brow, acromegaly was not present in this case. Psychological traits sometimes reported in males with the XXY and XYY karyotypes were seen in this patient, but the variability of expression of these characteristics calls into question the validity of their correlation with the presence of supernumerary sex chromosomes.

Case history

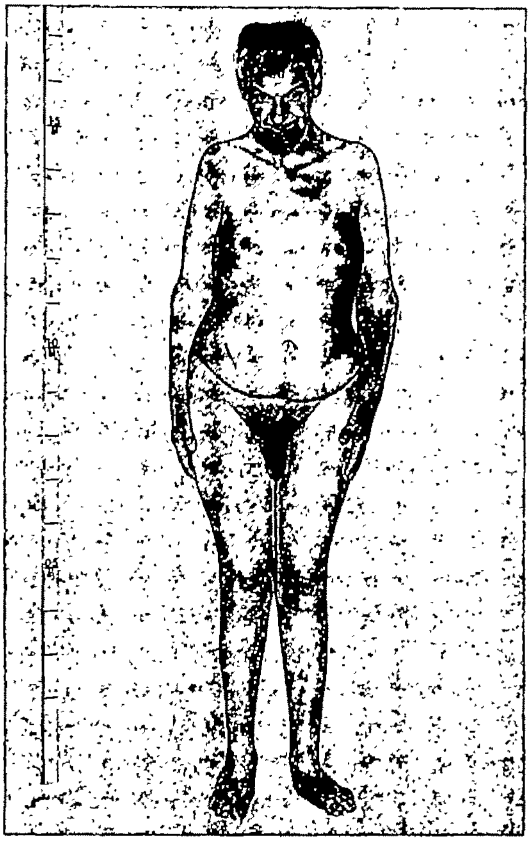
A 42 year old man with moderate mental retardation was discovered to have an XXXYY chromosome complement in the course of a cytogenetic survey of a hospital for the mentally handicapped.

He is the youngest of five sibs. His mother was aged 41 at his birth. Family members have refused to give blood for cytogenetic investigation but there is no family history of mental retardation.

He was admitted to the hospital at the age of 41 years. His early milestones are reported to have been reached in normal time, but at 10 months he contracted an illness resembling measles and thereafter he lost interest in his surroundings and did not walk or talk again until 7 years of age. He is reported to have been a child difficult to control at times, and to have been always solitary and "a loner". He was admitted to his present hospital when the surviving parent, his father, who looked after him, became ill.

He tends to shun company, be solitary, and is of a shy, passive disposition, but occasionally has outbursts of aggressive behaviour without apparent reason, suddenly hitting out at other people or breaking crockery or furniture. He appears to have episodes of depression when he is more withdrawn than usual, but it has been thought that these may have been a reaction to his mother's death and his admission to hospital.

Physical examination reveals an obviously mentally retarded man, 1.70 cm in height, moderately obese and of eunuchoid habitus, with wide hips and relatively narrow shoulders. His pubis-sole measurement is 86.5 cm. His voice is high-pitched. He has a very scanty growth of facial hair and no body hair except dimunitive patches of axillary hair and a small female pubic escutcheon. There is moderate gynaecomastia and a female distribution of body fat. The abdomen shows an appendicectomy scar. The penis is of normal size, but the testes are undescended. The hands and feet are small, with marked pes planus. There is some degree of genu valgum. There is a slight external strabismus of the left eye and a course tremor of both hands, but no other abnormalities on examination of the CNS. He is endentulous. He has a large and prognathic lower jaw, deeply set eyes and an overhanging frontal bone.



Discussion

The hypogonadal clinical features of Klinefelter's syndrome predominate in this man. This is consistent with other reported findings associated with the XXXYY sex complement which are summarised in the Table.

A projecting jaw and large hands and feet have been described in association with the XXYY sex chromosomal complement (Ellis, *et al.*, 1961). Similar findings in a case with the XXXYY complement were considered suggestive of acromegaly (Bray & Josephine, 1963). In this connection the prognathism and overhanging brow of the present patient may be noted, but these seem unlikely to be of significance as he showed no other signs that might indicate acromegaly. Prominent supraorbital ridges and prognathism, apparently in the absence of acromegaly, have been reported in another patient with an XXXYY sex chromosome complement (Salamanca-Gomez *et al*, 1981).

An infant with this karyotype has also been reported as having a somewhat prominent forehead and light prognathism (Lecluse-van der Bilt *et al.* 1974) and it will be interesting to see whether these features are seen in further cases.

From a psychiatric point of view, it is to be noted that in addition to mental retardation this patient showed psychological traits that have been observed in connection with Klinefelter's syndrome and in XYY males, although these traits are by no means a

TABLE

Manifestations of four males with 49, XXXYY chromosome constitutions

	Case of Bray & Josephine (1963)	*Case of Lecluse-van der Bilt et al (1974)*	*Case of Salamanca-Gomez et al (1981)*	*Present Case*
Age	26 yr	new born-3.5	29 yr	42 yr
Mental retardation	+	+	++	+
Hypogenitalism	+	+	+	+
Stature	192 cm	tall since 3.5 yr	176 cm	170 cm
Upper-to-lower segment ratio	0.89	—	0.91	0.97
Prognathism	+	+	+	+
Prominent cheek bones	+	—	+	—
Absence of facial, axillary, and pubic hair	+	child	+	±
Strabismus	—	—	+	+
Apparently short neck	+	—	+	+
Gynecomastia	+	child	+	+
Thoracic scoliosis	—	—	+	—
Small penis	+	+	+	—
Cryptorchidism	+	+	+	+
Paternal age	—	35 yr	44 yr	40 yr
Maternal age	20 yr	30 yr	38 yr	41 yr

constant finding and should not be regarded as specific concomitants always present (Slater & Cowie, 1971). Difficulty in establishing relationship with others, timidity, and a tendency to be withdrawn have been noted in Klinefelter's syndrome, and attention has been drawn to sudden outbursts of aggression against the background of a generally passive and apathetic personality in males with the XYY karyotype. The variability of these traits in Klinefelter and XYY males calls into question the validity of their correlation with supernumerary X or Y chromosomes, but in the present patient his timidity, tendency to be socially withdrawn, generally passive demeanour and sudden outbursts of aggression were marked features.

Acknowledgements

We thank Dr Elsarrag in whose care this patient is at Ely Hospital, Cardiff, for his kindness in allowing us to carry out investigations.

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*Valerie A. Cowie, MD, PhD, FRCPsych, *Senior Lecturer & Honorary Consultant Psychiatrist, University of Wales College of Medicine, Ely Hospital, Cardiff*

K. Rameshwari Singh, MBBS, DPM, *Clinical Assistant, South Glamorgan Health Authority, Ely Hospital, Cardiff*

Richard Wheater, BSc, *Cytogeneticist, Regional Genetics Service and Cytogenetics Unit, University Hospital of Wales, Heath Park, Cardiff*

*Correspondence

(*Accepted 24 June 1985*)

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Koro—A Psychophysiological Dysfunction?

F. OYEBODE, R. JAMIESON, J. MULLANEY and K. DAVISON

Koro or Su-Yang is a clinical syndrome characterised by the conviction that the penis is shrinking into the abdomen, and that if this is allowed to happen, it will result in death. There is associated panic, and preventive manoeuvres are instituted (Yap, 1951).

It was originally described as a culture-bound syndrome (Yap, 1951; Rin 1965), occurring mainly in the Far East in people of Chinese or Malay extraction. However, there have been a total of 17 cases reported in non-Chinese or Malay people, 15 of which were reviewed recently by Berrios & Morley (1984).

The central feature is the conviction that the penis is shrinking and this would amount to a delusion if it could be demonstrated that the grounds on which the belief was founded were false.

We wish to report a case which meets the criteria for the Koro syndrome, in which we conducted a penile plethysmographic study to validate the authenticity of his experience of penile shinkage. We are not aware of any other report in which such a study was carried out.

Case Study

GC, a 56 year-old man, initially presented in May 1975 with a six year history of recurrent shrinkage of his penis. The first episode occurred suddenly in 1969, whilst he was out cycling on a cold day; he had experienced a strange sensation in the perineum, and when he stopped to examine his penis, he was convinced that it had shrunk considerably. He had irregular recurrence of this "penile shrinkage" over the years, each episode lasting about 24–48 hours. The shrinkage was associated with the fear that his penis would disappear completely and that it was the sign of a serious illness. However, he never believed that it would prove fatal.

The episode provoked intense panic, during which he became restless and agitated; on one occasion, his wife hung onto his penis in order as he thought to prevent its total disappearance. The episodes were related to stressful situations such as holidays, difficulties at work, and entertaining at home.

He was born and raised on Tyneside and was an only child, whose mother committed suicide when he was 21 years-old; his father died 18 months later, and he perceived these parental deaths as particularly traumatic. He had been married for 26 years, and there were no children by choice. His pre-morbid personality was characterised by obsessional preoccupation with detail and an excessive concern for order and routine.

He was admitted in January 1984 when, in addition to a severe recurrence of his conviction that his penis was shrinking, there was also evidence of a depressive disorder with endogenous features. This was his first documented depressive episode, and its onset was dated to June 1983. The penile shrinkage had occurred over many years, without any associated depressed mood, and appeared to be independent of his depression. During this admission, his physical investigations, which included a Dexamethasone Suppression Test, were all within normal limits. The result of the penile plethysmography is reported below.

The penile complaint responded best to a combination of propranolol and thioridazine. It is of interest that lofepramine accentuated the severity of this complaint but the depressive disorder responded favourably to dothiepin. He has continued to be followed-up in the out-patient clinic.

Psychophysiological Study

Changes in penile circumference were recorded while the patient imagined shrinkage conditions, sexually stimulating images, and neutral stimuli. Recording was carried out using a mercury strain gauge, a Parks Plethysmograph (model 270), and a Wanatabe 4-Channel recorder. The DC amplifier on the pen was set at a gain of 0.2 volts/cm (later changed to 0.5 volts) and the paper speed was 30 mm/minute. The patient had, without prompting, shown his penis to the psychologist on two occasions, and he was not reluctant to carry out the experimental procedure. He was asked to put the strain guage on himself and stay fully clothed for the rest of the session. For the first ten minutes, he was encouraged to talk generally, whilst the balanced controls of the Plethysmograph was adjusted so that the pen stayed near the centre of the recording chart. This was equivalent to a penile circumference at 11.3 cm.

Whilst talking about sexual fantasies, he showed rapid fluctuations of penile circumference above the baseline (Fig. 1), which was indicative of an erection. The greatest increase was caused by voyeuristic fantasies; he was aware of having a partial erection whilst describing these.

Whilst describing an occasion when he was out cycling in cold weather and had experienced his penis shrinking, the plethysmograph recording showed fluctuations in penile circumference below the baseline (Fig. 2). He was aware of this as an experience of penile shrinkage.

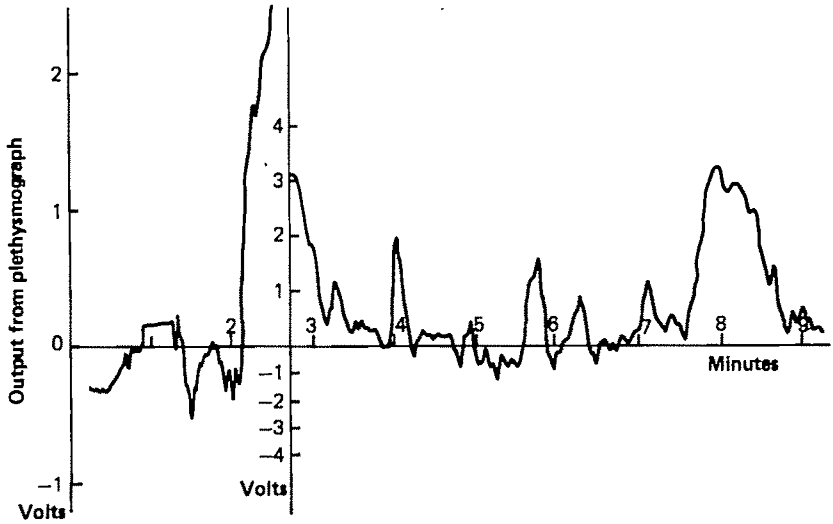

FIG. 1 Penile plethysmograph G.C. 17.1.1984 sexual fantasies.

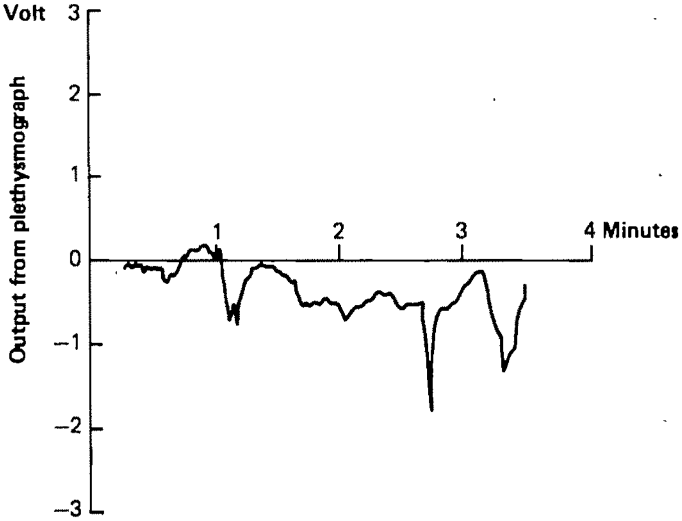

FIG. 2 Penile plethysmograph G.C. 17.1.1984 Cold fantasies.

Discussion

We have demonstrated in this case that the conviction of penile shrinkage corresponds with true physiological change in penile circumference below a baseline. This change is induced by specific imagery and therefore indicates that his conviction is not a delusion.

There are two possible explanations of our findings: Either this patient has dysfunctional autonomic control of his penile size, leading to more frequent or marked diminution in his penile size than would be normal, or, the changes in his penile size are normal, but his awareness is heightened by personal factors, such as obsessional self-scrutiny or sexual conflicts.

In the absence of normative data on changes in penile size in the normal male, we cannot reach any conclusions on the explanation in this particular case. It is not justifiable to extrapolate our findings to all cases which present with Koro, but further studies of this kind may increase our understanding of this condition.

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*Femi Oyebode, MB, BS, MRCPsych. *Senior Registrar in Psychiatry, St. Nicholas Hospital, Gosforth, Newcastle upon Tyne NE3 3XT*

Robin Jamieson, BSc, *Principal Psychologist. Department of Psychological Medicine, Newcastle General Hospital, Newcastle upon Tyne NE4 6BE*

James Mullaney, MB, BCh, MRCPsych. *Consultant Psychiatrist, Eastern Health Board, Grange Road, Raheny, Dublin, 5*

Kenneth Davison, FRCP, FRCP(Ed), FRCPsych., DPM. *Consultant Psychiatrist, Department of Psychological Medicine, Newcastle General Hospital, Newcastle upon Tyne NE4 6BE*

*Correspondence

(*Accepted 27 February 1985*)

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Correspondence

First Episodes of Schizophrenia

DEAR SIR,

We are pleased that Crow's group has been able to replicate our findings of a link between relatives' Expressed Emotion (EE) and the two year outcome of schizophrenia (*Journal,* this issue, pp 115–143), but are surprised at the negative way in which the results are presented. In addition there are some methodological defects in their replication which need pointing out. Of the 60 patients living in parental households, both parents were interviewed in only six cases. The convention in the EE research is to classify a household as high even if only one of the two parents is rated as high EE. The failure to interview one of the parents in such a high proportion of households must lead to a number of high EE households being incorrectly classified as low. Furthermore in 23 of the 72 patients successfully followed up, readmission was used as the outcome criterion instead of relapse, a problematic substitution. Despite these failings, the relapse rates recorded by Crow's group, 41% in low EE homes and 68% in high EE homes, are significantly different ($X^2=5.39$, $P<0.02$). Our own two year follow up is the most closely comparable study (Leff & Vaughn, 1981) but curiously MacMillan *et al* only quote our results for the subgroup who remained well at nine months. The whole group had two year relapse rates of 20% in low EE homes and 62% in high EE homes ($P=0.015$). The outcome for patients in high EE homes is closely comparable with that of Crow's group, whereas their relapse rate for low EE patients is substantially higher than ours. However this may be explained by their misclassification of some high EE households as low.

It is noteworthy that within the EE sample of patients studied by Crow's group, the two year relapse rates on active medication and placebo, 62% and 71% respectively, do not differ significantly ($X^2=0.50$). Furthermore, there is no association between EE status and allocation to active or placebo medication. It is therefore difficult to follow the logic of Crow's group in claiming that neuroleptic treatment partially accounts for the link between EE and outcome. Their assertion that acuteness of onset may mediate this relationship is another matter. We also found that acuteness of onset was linked both to EE status and to outcome. However, unlike Crow's group, when we conducted a log linear analysis we found that, taking acuteness of onset into account, the association between high EE status and poor outcome remained significant. They correctly state that the causal direction of the relationship between long duration of illness prior to admission and high criticism is unclear. It is conceivable, for example, that high EE relatives are more tardy in seeking professional help than low EE relatives. Even if high EE attitudes were provoked by an insidious onset of illness, it would not preclude a significant influence of relatives' attitudes on the course of schizophrenia. This kind of hypothesis has been tested by the four intervention studies cited by Crow's group, all of which have shown that altering family attitudes produces a major benefit for patients over and above the protection afforded by maintenance neuroleptics. In our own study (Leff *et al*, 1985) the relapse rate of control patients in high EE homes who took regular medication was 78% over two years, very similar to the comparable rate of 86% recorded by Crow's group (Table IV). In our trial, social intervention reduced this to 20%. This could not possibly be due to better compliance with medication, which Crow's group suggest as an explanation for similar benefits achieved by Falloon *et al* (1985).

We must also comment on the high proportion of immigrants in the Northwick Park sample who could not be interviewed for EE assessments. A recent study of first contact schizophrenic patients in Chandigarh, India, has shown that not only are the EE techniques applicable to a Hindi-speaking population, but that they also predict relapse in this very different cultural milieu (Leff et al, in press).

Finally, the review of the literature on EE compiled by Crow's group includes a number of inaccuracies and we will address these issues in this *Journal* at a later date.

JULIAN LEFF

Friern Hospital
Friern Barnet Road
London N11

CHRISTINE VAUGHN

Prestwich Hospital
Manchester M25 7BL

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Monoamine Oxidase Inhibitors

DEAR SIR,

Dr Pare's article on 'The Present Status of Monoamine Oxidase Inhibitors' is one of a genre that marks the renaissance of these drugs (Murphy *et al*, 1984; White & Simpson, 1985).

This is understandable given that the 'second generation' compounds are less exciting than hoped, that early use of phenelzine was often with inadequate dosage and that improved diagnostic criteria give some (still scanty) hope that the elusive 'MAO' responder might be found.

There appears also to be a naive and wishful assumption that because their therapeutic potential may have been underestimated the side effects of MAOI were exaggerated. It would be more logical to conclude that adequate dosage and effective treatment might also increase the incidence of side effects above placebo level.

This point may be illustrated by referring back to the original work that Professor Marley and I conducted during a three year period, more than 20 years ago (Blackwell *et al,* 1967). A careful epidemiologic assessment of the risk for hypertensive crises in the contained population of a single hospital revealed that 8% of patients on tranylcypromine experienced the problem compared to 1·5% of those on phenelzine. Analysis of prescribing data showed that episodes on phenelzine occurred at higher dosage after longer duration of treatment, suggesting what has now been confirmed about the significance of adequate treatment. This observation was used as the basis for a carefully conducted clinical pharmacology experiment in which the hypertensive effects were shown to be related to the duration of treatment, proximity and dosage of phenelzine antecedent to a food challenge.

A recent prospective controlled comparison (Rabkin *et al,* 1984) was made of the incidence of serious side effects in patients taking phenelzine, imipramine or placebo. Like the earlier study (Blackwell *et al,* 1967) it was conducted in a university research clinic by experts in psychopharmacology.

The incidence of hypertensive crisis on phenelzine was exactly the same (8%) as previously reported with tranylcypromine. Eleven patients suffered a hypertensive crisis of whom six ate tyramine containing foods 'despite meticulous dietary review and cautioning' and three took ephedrine-containing medication. Four of the eleven patients obtained emergency medical treatment and a fifth was hospitalised in coma with intracranial bleeding due to an unsuspected aneurysm.

What may happen in less carefully supervised environments is suggested by a report from a British counseling service (Wright, 1978). Despite warnings about foodstuffs and cold remedies thirty-five out of one hundred and nineteen patients suffered hypertensive crises of which four were fatal.

Wide discrepancies in the reported incidence of side effects are contributed to by pendulum swings from early over-reporting to later under-reporting. The way to truth is not to average good and bad data (gleaned from meaningless prescribing statistics and manufacturers myopic files) but to sift the wheat from the chaff. Based on the (to my knowledge) only 2 carefully conducted studies my own conclusions differ markedly from Dr Pare's view that the risk of hypertensive crisis has been exaggerated. These conclusions are:

1. In carefully observed university settings patients treated with adequate therapeutic dosages of an MAOI and warned to avoid foodstuffs and ephedrine medications the risk of hypertensive crisis is 1 in 12 (8%).
2. It is impossible to predict which individual patients will be compliant (Blackwell, 1976) but about half will have unavoidable memory lapses. Fear-provoking messages are not likely to reduce the problem since they often facilitate forgetting.
3. Any patient with adequate MAO inhibition will experience hypertension if he ingests enough tyramine or any of the indirectly acting amines. A majority of these will remain unaware of raised blood pressure but a small minority will suffer serious consequences.

The risks of MAO inhibitors are not confined to this one side-effect. In the study cited above (Rabkin *et al,* 1984) the incidence of severe side effects was 14% on placebo, 27% on imipramine and 64% on phenelzine. With phenelzine these were hypomania (10%), hypertensive crisis (8%), weight gain over fifteen lbs. (8%) and anorgasmia or impotence (22%). Treatment over time revealed that by thirty-three weeks less than half the imipramine patients suffered a serious side effect compared to over 90% of phenelzine treated patients. Thirty eight per cent of patients had two or more serious side effects and all except one were taking phenelzine. Altogether 132 major side effects were recorded for 141 patients treated with phenelzine.

The risks of MAO inhibitors will be further increased in an era of 'prophylaxis' and long-term treatment. Recent studies have shown that withdrawal effects are more serious than with tricyclics (Tyrer, 1984) and overdose is extremely difficult to manage (Linden *et al*, 1984).

The most remarkable feature of the above study was that in a second article (Rabkin *et al*, 1984) the authors were able to conclude that 'MAO inhibitors when properly prescribed are safer than is often believed'. This chemophilic conclusion seems to be supported by Dr. Pare's treatment of the risk to benefit ratio for these drugs. For the sake of the patients to whom we prescribe I hope that a more careful view will prevail so that we learn from the lessons of history without repeating them. This is the second time around for the MAO inhibitors but the millenium has not arrived.

Barry Blackwell
University of Wisconsin Medical School
Milwaukee Clinical Campus

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Cyproheptadine and Antidepressant-induced Anorgasmia

Sir,

Anorgasmia in women is a recognised side-effect of clomipramine (Anafranil data sheet) and has been reported with imipramine (Sovner, 1983). We report two cases of anorgasmia, one induced by clomipramine, the second by imipramine, which resolved with cyproheptadine. A third patient who had imipramine-induced anorgasmia failed to respond to this treatment.

Case 1: Mrs E. T., aged 36 years was prescribed clomipramine for depression. The dose was started at 25 mg nocte and increased to 75 mg. Within two weeks of starting this treatment she experienced anorgasmia. She could become sexually aroused but was unable to achieve orgasm either during intercourse or by masturbation. This situation had persisted for three months during which time clomipramine 75 mg nocte was continued. A reduction to 50 mg nocte did not improve her sexual functioning. She continued to take clomipramine 50 mg nocte and was given a supply of cyproheptadine 4 mg tablets with instructions to take one tablet ninety minutes before anticipated sexual activity. If after trying this on four occasions she was still anorgasmic she was to progressively increase the dose. The first time that she took 8 mg cyproheptadine she experienced orgasm in response to masturbation. So long as she takes cyproheptadine 8 mg before sexual activity she is orgasmic. She failed to achieve orgasm after taking placebo tablets which she was told were cyproheptadine 8 mg.

Case 2: Miss A. C., aged 22 became depressed after a broken love affair. She was treated with imipramine, starting with 25 mg nocte and increasing to a total daily dose of 100 mg. Within a week of increasing the dose to 75 mg she experienced anorgasmia during masturbation, her only form of sexual outlet. She had previously been multi-orgasmic and had regularly masturbated 3–4 times a week. She continued to take imipramine 100 mg daily and was given a supply of placebo tablets. She was told to take these tablets ninety minutes before masturbation, increasing the dose from one to four tablets. This did not resolve the anorgasmia. She was then started on cyproheptadine and became orgasmic when she took 12 mg before masturbation (the placebo tablets did not match the active tablets).

Case 3: Mrs W. M., aged 28 had been taking imipramine 150 mg daily for depression for six months. During this time she consistently failed to achieve orgasm. Before starting this treatment she was coitally orgasmic on about 50% of occasions. She was given placebo tablets and then cyproheptadine tablets as in Case 2. Neither the placebo nor cyproheptadine 8 mg resolved the anorgasmia. Drowsiness induced by the cyproheptadine prevented further increments in dose. Desipramine 100 mg daily was substituted for the imipramine but this change of treatment did not resolve the anorgasmia. She was then weaned off anti-depressants and again became orgasmic.

The physiology and pharmacology of sexual function are poorly understood. Animal studies have implicated a 5-hydroxytryptamine (5HT) as one of the likely neurotransmitters involved in the control of sexual responses, and this amine probably has an inhibitory role. Clomipramine and imipramine inhibit the re-uptake of 5HT, but also exhibit anti-cholinergic and alpha adrenoceptor antagonist activity. Cyproheptadine is a 5HT receptor antagonist. In two of the three cases reported cyproheptadine reversed the inhibiting effect of the anti-depressant on orgasm. These observations suggest that anti-depressant-induced anorgasmia results from the effect of these drugs on 5HT activity. Sovner (1984) also reported a case of tricyclic anti-depressant-induced anorgasmia which was reversed by cyproheptadine. More recently, Decastro (1985) successfully reversed MAOI-induced anorgasmia in a male with cyproheptadine.

In Case 3 the patient was prevented from increasing the dose of cyproheptadine by the occurrence of side-effects. Treatment with imipramine was changed to desipramine because Sovner (1983) reported the case of a woman who experienced anorgasmia with imipramine but not with desipramine, but in our case this change of treatment was ineffective in restoring orgasmic attainment.

ALAN J. RILEY
ELIZABETH J RILEY

Touchwood House,
Wendens Ambo,
Saffron Walden, Essex

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Depression and Urinary Free Cortisol

DEAR SIR,

The article by Dr R. J. Dolan and colleagues, "Life events, depression and hypothalamic-pituitary-adrenal axis function" (*Journal*, October 1985, 147, 429–433) reports some differences in urinary free-cortisol excretion between patients with and without severe life events or with and without marked difficulties.

It seems important to point out, however, that the actual 24 hour urinary free cortisol (UFC) excretion values (µg/24 hours) were unusually high in all these patients, whether or not adverse life events and difficulties were present. All the mean values are greater than 145 µg/24 hours. In most other studies the mean UFC excretion of normal subjects is about 40 to 50 µg/24 hours and in depressed patients the values rarely exceed 100 µg/24 hours (Carroll *et al*, 1976). The values given by Dr Dolan and associates are all well within the range expected for patients with Cushing's disease.

The authors stated that they used a radioimmunoassay procedure for their UFC analyses. The results call into question the validity and specificity of their assay or of the laboratory procedure they adopted. These considerations also would tend to raise questions about the validity of their plasma cortisol assays for assessing DST status of the subjects (Ritchie *et al*, 1985).

Radioimmunoassays for cortisol vary widely in their performance. For this reason, validation of the assay by establishing local norms always is to be encouraged.

BERNARD J. CARROLL

Duke University Medical Center
Durham, North Carolina 27710

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Complaints of Inability to Sneeze

DEAR SIR,

Shukla (*Journal*, November 1985, 147, 564–565) suggests asneezia as a previously unrecognised psychiatric symptom, yet fails to distinguish between the patient with a genuine absence or reduction in frequency of sneezing and the patient who complains of such but in whom there is no objective change. In the absence of this distinction, an alternative explanation is that he is reporting culturally determined hypochondriacal overvalued or delusional ideas. The following observations support this view.

Firstly, Dr Shukla highlights the importance of sneezing within Indian culture and it is well known that the content of such ideas is culturally dependent (Hamilton, 1974). Secondly, there were significant differences between the educational and socio-economic backgrounds of the asneezic and the control groups, and it has been widely suggested that patients of lower socio-economic groups and educational achievement are more likely to present with somatic complaints (Connolly, 1979). Thirdly, hypochondriacal delusions occur in up to a fifth of schizophrenic disorders and are well known in affective disorders (McKenna, 1984) and these formed the majority of the asneezic group. Finally, the long duration and poor prognosis of such ideas in non-psychotic patients is well recognized (McKenna, 1984) and this is also in keeping with Dr Shukla's results. This would suggest that any further research be confined to the confirmation of asneezia as a genuine symptom. Only then can one consider the various biochemical hypotheses raised by Dr Shukla.

ANDREW CLARK

Fleming Memorial Hospital
Great North Road, Newcastle upon Tyne NE2 3AX

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Seasonal Variation in Suicides for Males and Females.

DEAR SIR,

There has been a recent series of papers in this *Journal* on the seasonal variation of suicide in males and females. In general, the papers (Meares *et al*, 1981; Nayha, 1982; Parker & Walter, 1982) find a spring peak for males and spring and autumn peaks for females.

I should like to note that in the *Journal* (Lester, 1971), I reported on the seasonal variation in suicidal deaths in the USA and found a variation over the months of the year that was significant for males, for those using active methods of suicide and for those aged 55 and over, but not for females, those using passive methods, and those aged 15–54. In a later article (Lester, 1985), I found the Spring peak for most methods of suicide, but the Autumn peak only for those using poisons.

Since the shape of the seasonal variation may vary with method for suicide, and age, as well as sex, these other variables must be controlled for before we can conclude that the sex difference is a reliable and valid phenomenon.

DAVID LESTER

Stockton State College
Pomona, New Jersey 08240

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Lithium in Resistant Depression

DEAR SIR,

In their carefully presented paper, Drs Schrader and Levien (*Journal*, November 1985, **147**, 573–575) have not in our view proved their point.

Could not the improvement have been the result of giving the lithium carbonate alone independently of whatever had previously been administered to the patient?

SAMUEL I. COHEN
B. A. JOHNSON

The London Hospital Medical College
Turner Street, London E1 2AD

CORRECTION

In the paper by Drs Birtchnell, Lacey and Harte 'Body Image Distortion in Bulimia Nervosa' (*Journal*, November 1985, **147**, 408–412) the paragraph on page 410 referring to Table IV should read as follows:

As is illustrated by Table IV, the distortion of body perception in bulimics increased with deviation of weight index from 100%. The statistical comparisons that follow were made between the heavier intermediate group and the heaviest groups with the lighter intermediate group (normal weight index 95–105%) rather than the lightest group as published.

British Journal of Psychiatry (1986), **148**, 220–225

Book Reviews

Object Relations: A Dynamic Bridge between Individual and Family Therapy. By Samuel Slipp. New York: Jason Aronsen. 1984. Pp. 270. $27.50.

The aim of this book is to demonstrate that the antagonism between psychoanalysis and family therapy is misconceived and is to the detriment of both parties. Dr Slipp successfully shows how his version of object relations theory can be employed to establish a complementarity between the two approaches. He arrives at formulations which seem more veridical and serious than is often the case in this field.

However, his reconciliation of the two parties is accomplished at the cost of considerable casualties. The trouble starts early on in that it is crucial to his argument that psychoanalysis emphasises the intrapsychic and almost completely obliterates the interpersonal. To justify this assessment of psychoanalysis the book espouses an idiosyncratic reading of Freud which at many points is over-simplified, uninteresting and wrong. It denies the fact that relationships between people, including family members, are fully recognised in clinical psychoanalysis.

Dr Slipp's account of the basis of different types of family therapy is much more impressive but when it comes to object relations theory there are a number of mistakes. Ferenczi is described as the "progenitor of object relations theory". Melanie Klein's emphasis upon the infant as having to cope with powerful instinctual feelings of love and hate is almost totally ignored. It is wrongly asserted that, "the later part of the depressive position is considered to be the fixation point for borderline and narcissistic disorders".

The central thesis of the book employs a notion of projective identification. It is argued that children become ill as a consequence of playing out aspects of the parents' personalities. The parents have not achieved true integration, instead their psychic economy is precarious requiring the child to embody disavowed aspects of their personalities in order to maintain a semblance of stability. This enactment is accomplished by various unconscious manoeuvres to influence the child. Families of this sort display a "symbiotic survival pattern". These patterns are specific for schizophrenic, depressive, hysterical, borderline and delinquent pathologies. These different family typologies are described.

There is much evidence to support the contention that family relationships are significant in the genesis and maintenance of these disorders. The family therapists have made original contributions in suggesting the ways in which this may be so. However, whilst there are novel aspects to Dr Slipp's family typologies, I find the patterns he describes over-simplified and ill-substantiated. There is a neglect of the basic components and structure of the mother/infant relationship as well as other family relationships. The powerful contribution made by the nature of the child, and the child's impact upon the parents and family is not mentioned. To his credit Dr Slipp does not display the gross naivety of some family therapists yet I still felt that the enduring interactability of character and pathology was underestimated.

One is basically in sympathy with Dr Slipp's approach and parts of his book are very valuable. He is surely right that the interpersonal and intrapsychic are intimately interrelated but, equally, it takes us little further merely to assert that.

Family therapy is an exciting development which has made a number of novel and original suggestions. There are areas of agreement with psychoanalysis and areas of profound difference and it awaits for more detailed work to formulate and resolve these issues.

DAVID TAYLOR, *Consultant Psychotherapist, Tavistock Clinic, London*

Physiological Correlates of Human Behaviour. Edited by ANTHONY GALE and JOHN A. EDWARDS. Vol. 1; **Basic Issues.** Pp. 350. £25.00. 1984. Vol. 2: **Attention and Performance.** Pp. 245. £25.00. 1983. Vol. 3: **Individual Differences and Psychopathology.** Pp. 298. £28.00. 1984. Orlando, Florida: Academic Press.

Gale and Edwards are to be complimented on bringing together such a rich mixture of papers in biological experimental psychology. Working on the premise that the study of neurophysiology must necessarily encompass the whole gamut of psychological systems the editors have collected some 40 contributions, in three volumes, to represent the range and diversity of the physiological correlates of human behaviour.

There is something of interest for both tyro and expert within the 900 pages of these books. The editors have not forced a uniform mould upon the contributors and the large inter-author variation in style and content makes for easy reading. The individual papers are of a uniformally high standard with respect to the information presented and a serious attempt has been made to demystify and simplify some of the more complex concepts in polygraphy, psychometrics, psychophysiology, psychopathy, chronopsychology and "arousal".

A reviewer's choice of papers must obviously reflect his particular interests. It is good to find that I do not have a favourite volume and my preferred papers are spread throughout the collection. Perhaps the strength of these books lies in the way in which important issues—at least as I see them—like memory, cognitive ability and information processing are dovetailed together throughout the three volumes with one contribution augmenting another. For example, 'Information Processing' (J. Boddy, Vol. 1) and the 'Neurochemistry of Learning and Memory' (D. Warburton, Vol. 1) are excellent precursors to 'Memory and Arousal' (M. Eysenck, Vol. 2) and 'Cortical Correlates of Intelligence' (Gale & Edwards, Vol. 3).

Similar inter-volume links occur with topics in neuropsychology, pathophysiology and experimental methodology. The 'Cinderella' corner contains fascinating chapters on 'Sexual Arousal in the Human: Love, 'Chemistry or Conditioning?' (Vol. 1): 'The Psychophysiology of Aesthetics' (Vol. 2) and 'Psychopathy, Delinquency and Crime' (Vol. 3). Within each volume there is little to suggest that much thought was given to the order of the chapters and the whole is best regarded as a set of monographs which, nevertheless, reflect most of the important areas of physiology and behaviour. It is, however, necessary to change cognitive set rather rapidly in instances when one reads in sequence contributions on 'Personality', 'Pain', 'Intelligence', 'Sensation Seeking' and 'Evoked Potentials'! Although each volume has an adequate subject index I feel it would help locate important topic areas if the whole three volumes were indexed together.

It is evident that these volumes have been designed to be 'dipped into' and read by those interested in any clinical psychological, sociological or theoretical aspects of the psychophysiological basis of human behaviour. The apparent lack of internal organisation in the sequencing of the chapters and, of course, the high cover price might mitigate against the use of these books as student texts. As source books for 'further reading' I doubt if they could be bettered at either an undergraduate or postgraduate level.

Such an extensive work with its many and varied contributions must be, to many readers, somewhat like the curate's egg: good in parts and not so good in others. The parts of these three volumes are never "bad". In certain parts there are excellent and well written chapters to be found and they can be recommended to anyone desirous of reading about those aspects of psychophysiology which are relevant to human behaviour.

IAN HINDMARSH, *Head of Human Psychophopharmacology Research Unit, University of Leeds*

The Mental Status Examination in Neurology. RICHARD L. STRUB and WILLIAM BLACK. 2nd Edition. Philadelphia: F. A. Davis. 1985. Pp. 232.

The recognition and assessment of defects of higher cerebral function is clearly a fundamental part of the assessment of patients with diseases of the brain. The problems faced by neurologists and psychiatrists differ and the approach to examination of the higher functions of the brain is determined by the differing perceptions of brain function. The neurologist is primarily interested in establishing a functional and anatomical diagnosis and, as such, is interested particularly in quantitative assessment of aspects of perception and motor function, especially including the results of tests of abstract thought processes relevant to behaviour. The domain of hallucinatory behaviour and disordered thought processes representing results of introspective enquiry are of less value to the neurologist than the psychiatrist. Clinical psychology, however, is a discipline that overlaps both these requirements and, as such, is sometimes perceived by neurologists as producing results not strictly relevant to their clinical practice. There has long been a need for a reasonably concise text summarising the position of the neurologist with regard to these problems of the assessment of higher mental function. This book, now in its second edition, fulfils this need admirably. It presents the methodology and attitude of the Boston school of thought concerning higher cerebral function in a didactic form. Areas of controversy are simplified so that a strictly localisationalist approach is taken. This approach has many advantages and, because of the pattern of references chosen, the reader can accept this view for the purposes of lesion making and understanding the basic principles of aphasia assessment, and the investigation of apraxia and agnosia. The authors freely admit, in the text, that the more eclectic approach taken by psychiatry, and by other schools of neurology, has not fallen within their approach. Thus, a strictly hierarchical account is given of frontal lobe functions and there is relatively little about non-verbal abstract behaviour.

Throughout the book, much emphasis is placed on the virtues of routine analysis of mental functions in neurological practice, particularly on the acquisition of skills by practice and on the assessment of mental function using shortened forms of the various standard tests. The book is loosely divided into introductory sections, followed by chapters concerned with language, consciousness, attention, memory, instructional ability, agnosia and apraxia. The concluding chapter provides succinct and abbreviated accounts of the role of most of the neuropsychological tests commonly used by clinical psychologists but, unfortunately, there is no attempt to integrate the results of these more formal assessments with the tests used by the neurologists. The book does perhaps suffer a little from regarding depression as a complication of neurological disease rather than an entity in itself and most neurological readers would greatly benefit from a clear account of the abnormalities of behaviour and perception found in patients with depressive psychosis. In addition there is no advice as to how to assess children and the concept of mental retardation, and its influences on the tests described, is not to be found in the book. The neuropsychological assessment of patients is greatly modified by innate mental ability, and by brain lesions acquired in infancy and in the perinatal period and the assessment of such defects represents a common and difficult problem. Nonetheless, this book will be greatly valued by neurologists, particularly those in training, and will provide a useful summary of neurological thought concerning the localisation and concept of brain function for neuropsychologists and psychiatrists.

MICHAEL SWASH, *Consultant Neurologist, The London Hospital (Whitechapel)*

Essentials of Child Psychiatry. 2nd edition. By H. M. CONNELL. Oxford: Blackwell Scientific. 1985. Pp. 344. £9.80.

The second edition of Connell's book has been extensively updated with many topics expanded considerably. School problems have been separated into a chapter of their own and a chapter on forensic child psychiatry added. The book has been increased in length by nearly a third. Sections on epidemiology, lack of mothering, classification, psychological testing, affective disorders, hyperkinesis, substance abuse and suicidal behaviour have been considerably lengthened. Much new research is reported and the book well deserves to be seen as a new edition rather than a slight revision of the first. The layout has been changed in places to make understanding clearer.

As in the first edition, the author refers frequently to research findings. There is no particular school of thought that dominates. Psychodynamic, learning, and family systems theories are all well balanced together. The book reads well, covers a great deal of ground, is clear, and gives an excellent understanding of many of the emotional problems and stresses that children and families in a very diverse number of situations may experience in their life and development. The illustrations of children's drawings are well chosen and explained; there are relevant and helpful case descriptions.

For a book so well thought out and comprehensive there remains a serious gap still left in the new edition. Whereas hyperactivity receives 11 pages and school refusal five, truancy is discussed in eight lines and disobedience, aggression, and stealing have no separate space at all. The section in the previous edition more appropriately entitled 'Delinquent Behaviour' has been expanded and retitled 'Conduct Disorders', but fails to look at the troublesome but non-delinquent behaviour problems so commonly seen in the child psychiatry clinic. This makes the book less useful than it would be if the conduct disorders had received the same care and attention as some of the problems so well described in other sections.

In summary an excellent and recommended introduction to the psychological problems of childhood in a well updated and revised second edition. It is clearer, less dogmatic, and more research-based than many of its competitors. A little more on conduct disorders next time, please.

JOHN BARCROFT, *Consultant Psychiatrist in Child and Family Psychiatry, Cambridge*

Children's Group Therapy. Methods and Case Histories. By MORTIMER SCHIFFER. New York: The Free Press. 1984. Pp. 403. $30.00.

The author of this book, intended as a clinical handbook of group therapy with children, is a clinical psychologist who draws on 40 years of clinical practice. He was clearly much influenced by his mentor the late S. R. Slavson, a pioneer of this approach, and includes chapters by him and a number of other colleagues.

The book is divided into five clear parts each with a description of underlying theory followed by detailed case material to illustrate the points made. Part 1 describes "activity group therapy", a play group approach for quite young children with an emphasis on permissiveness and acceptance on the part of the therapist. Part 2 "activity interview group psychotherapy" designed for a slightly older age group is a similar play situation but allows for more discussion and some interpretation by the therapist. The third and fourth parts cover "combined treatment" that is, activity groups as well as individual therapy and "co-operative therapy", adding therapy with a parent to work with the child. The final, and in some ways most helpful part deals specifically with a group approach to children with "severe ego impairment", those we all recognise as most difficult to help.

All sections emphasise the need for regular sessions over several years and all point out the value of including a snack meal in each group session. There is a most useful short appendix describing desirable room size and layout and suitable play and craft materials. The age groups covered are mainly pre-puberty.

This would be a helpful starting point for any professional interested in this approach and it is easy to read in spite of the frequent use of analytic terminology. Some of the case material, particularly in Parts 1 and 4 is excessively detailed and thus rather dull to read, and there is an overall dated feel about the book. The comprehensive bibliography is helpfully laid out in sections covering different possible group settings; schools, hospitals etc.

PATRICIA AINSWORTH, *Lecturer in Child and Adolescent Psychiatry, University of Manchester*

Childhood Psychosis in the First Four Years of Life. By HENRY N. MASSIE and JUDITH ROSENTHAL. Maidenhead: McGraw-Hill. 1984. Pp. 315. £18.95.

The authors address themselves to the crucial question of the behaviour and development of infantile psychotic children prior to the onset of psychosis. In addition to the descriptions of the syndrome they address themselves to origins and processes in the first four years of life. Their method is unique and innovative and they undertake systematic analyses of home films that families had made of the infancy of children who were later found to have a psychotic disorder, and compare these with normal children. They compare 14 psychotic and 14 normal control children using carefully defined rating scales that examine cognitive development in relation to Piaget's sensori-motor stage and also affective development and attachment behaviour. These ethological-type observations are complemented by case studies. The orientation of the authors is psychodynamic and inevitably they offer a psychogenic explanation for childhood psychosis (including autism!). Nevertheless, their ideas and inferences are thought-provoking.

The remainder of the book is devoted to more familiar themes: overviews of historical background and of classification of childhood development from the perspective of mother–child interaction. There is a chapter on treatment of childhood psychosis—which raises more questions than it answers. These latter sections are somewhat thin on the ground in that they lack substantive reference to the similar themes which have been better tackled elsewhere in the UK and USA literature. A useful appendix provides the Massey-Campbell Scale of Mother–Infant Attachment.

The book is well written and is moderately priced. However, its value tends to be limited to the accounts of the features which precede the diagnosis of psychosis—some of which may constitute early predictors.

TRIAN FUNDUDIS, *Principal Clinical Psychologist, Nuffield Child Psychology and Psychiatry Unit, Newcastle upon Tyne*

Obsessive–Compulsive Disorder: Psychological and Pharmacological Treatment. Edited by MATIG MAVISSAKALIAN, SAMUAL M. TURNER and LARRY MICHELSON. New York: Plenum Press. 1985. Pp. 257. $29.50.

The editors describe their book as integrating and synthesising the conceptual frameworks and treatment modalities which have arisen from recent advances in behavioural and biological treatments.

There is evidence throughout of efforts to address these aims, but it is disappointing that, overall, a relatively small proportion of the book is concerned with them directly. Far too much space (almost exactly half the book) is devoted to two chapters reviewing clinical and research issues (S. J. Rachman) and behaviour therapy (E. B. Foa, G. S. Stekatee & B. J. Ozarow). As usual, in both cases, presentation is masterly but unfortunately the content is predictable and familiar, a great deal of it being readily available in their previously published works. The omnipotence of their own behavioural conceptual framework is assumed with only scant reference to possible integration with alternative models and treatment techniques.

The remaining four chapters are variable both in quality and in style. J. Ananth's contribution on pharmacotherapy shares some of the characteristics of the two just described in that well presented review takes precedence over discussion of synthesis of alternative approaches. The chapter on short-term dynamic psychotherapy (P. E. Sifneos) may be of limited relevance as the patients described are atypical. Therefore, there is an omission of any full consideration of the role that psychotherapy could play, which is not entirely redressed in L. Salzman's brief chapter on psychological treatment.

Finally, in the concluding chapter, the editors do attempt to integrate the preceding contributions and they provide some interesting formulations, redefining and clarifying the essential features of the obsessive–compulsive complaint.

In summary, this book provides a sound and thorough review of conceptual models and treatment approaches. It fails to make the stimulating and innovative contribution to thought on obsessive–compulsive disorder that its stated aims invite.

MARGARET VAUGHAN, *Principal Psychologist, The David Lewis Centre for Epilepsy, Warford, Cheshire*

How Does Analysis Cure? By HEINZ KOHUT. London: University of Chicago Press. 1984. Pp. 240. £21.25.

This third and last book of the late Heinz Kohut is a further discussion of his work as a psychoanalyst with patients with narcissistic disorders. It is partly a reply to various criticisms made by other psychoanalysts of his two other books, *The Analysis of the Self* and *The Restoration of the Self*, and partly a discussion of how psychoanalysis may be curative. It was edited after Kohut's death by Arnold Goldberg and Paul Stepansky.

Some understanding of Kohut's thinking about the psychopathology of the self would help the reader. Kohut was preoccupied with understanding those ways in which a child's early sense of self might be disrupted or distorted not only by what the parents did to him but by the ways in which their presence was felt. Kohut felt that these early disruptions of the self might lead to an extreme vulnerability to narcissistic injuries in later life, in which a person might lose touch with the sense of his own humanness and worth. Kohut's conception of 'self psychology' led him to develop new ways of working with his patients with such disabilities. Thus, he came to place a greater emphasis on the mirroring function of himself as analyst in helping his patients to find an endorsement of and recognition of a re-emerging sense of self. This led to various criticisms, including one that he might merely be advocating an analytic collusion with his patients' misperception of their environment. His answer to this and the other criticisms are set out in the first part of this book. In the second part he develops his ideas of what constitutes a psychoanalytic cure and how it may be achieved. What emerges is a deeply tolerant and informed view of the individual's possibility for growth that is somewhat less absolute in its demand upon the therapeutic situation than certain other psychoanalytic approaches. Kohut's view that the analyst may need to be prepared to acknowledge his own empathic failures when reproached by his narcissistic patients, is a refreshing one.

This is not an easy book to read because its style is so laboured but it helps throw further light on the thoughts of a compassionate and original man.

PETER SHOENBERG, *Consultant Psychotherapist, University College Hospital, London*

Ethics in Clinical Psychology. By JANE STEERE. South Africa: Oxford University Press. 1985. Pp. 125. £8.95.

The author of this small but comprehensive book introduces her subject by stating: "In general in professional ethics, the over-riding principle is that the client's interests are given priority above the interests of all others. This is intended to provide assurances to clients that the professional will not allow his own self-interest or the competing claims of others in society to prejudice the client's chances of receiving the best possible treatment" (p. xiii). Against this background and her review of the development of clinical psychology as a profession, she provides a brief but thorough discussion of the philosophy and process of ethical decision-making in relation to clinical psychology. She discusses utilitarian and deontological ethical theories, emphasises the widely held ethical principles of respecting the client's autonomy, of non-maleficence and beneficence, and describes difficulties involved in solving ethical dilemmas. Later chapters are concerned with the application of ethics in psychotherapy, psychological assessment, research, legal proceedings, professional conduct and professional relationships. These chapters offer a valuable introduction and important guidelines to ethics in clinical psychology.

The final chapter is entitled 'The South African Context'. Steere uses Maslow's hierarchy of needs to show how the South African racist system discriminates against blacks on *all* levels; on physiological security and safety needs, affiliation and belonging, personal esteem, learning, aesthetic and self-actualisation needs. She describes how this situation inevitably leads to poor mental health among blacks. The chapter is an eloquent condemnation of an inhuman and unethical political system. The book is worth acquiring for this chapter alone.

PETER BUTCHER, *Principal Clinical Psychologist,*
The London Hospital (Whitechapel)

The Development of Personal Construct Psychology. By ROBERT A. NEIMEYER. London: University of Nebraska Press. 1985. Pp. 172. £18.95.

This unusual book presents a socio–historical analysis of personal construct psychology (PCP), using an approach derived from N. C. Mullins, whose 1973 model described four successive stages of theory development.

The initial 'normal' stage ended with G. Kelly's 1955 publication of 'the psychology of personal constructs', expressing the developed views of the theory's originator. This catalysed the 'network' stage as Kelly's students dispersed and created satellite units. As these enlarged, they formed 'clusters' which evolved into the 'specialty' stage.

The application of this model is interesting and will be novel to many readers of this journal. It is of some interest—at least to those with some involvement in PCP—to note that psychiatrists have been involved in the field in UK, but not elsewhere. Not satisfactorily, I hasten to add, in terms of sound adherence to PCP theory, according to some UK PCP psychologists. Such sub-school foundation is typical of 'specialty' status of a theory and familiar in relation to many other frames of reference current in recent years—psychoanalysis, behaviourism, social psychiatry, psychopharmacology—and as unprofitable in them as in PCP.

I thought this book's coverage was admirably complete except that the potentially important work with computer-interactive PCP and grid work developed by L. Thomas and M. Shaw is omitted. The general message reminding us that a theory is a construction of its time and social space is worth the attention of a wide psychiatric audience.

J. P. WATSON, *Professor of Psychiatry,*
United Medical and Dental Schools
(Guy's Hospital), London

The Psychopharmacology of Epilepsy. Edited by MICHAEL R. TRIMBLE. Chichester: John Wiley. 1985. Pp. 184. £21.50.

Another multi-authorship book, but with many of the snags of this type of publication overcome, for which the editor is to be warmly congratulated. It is not based on a conference, is relatively brief, and the chapters concise. There is an excellent introduction, and what is so often lacking in such a publication, an equally good conclusion. The editor contributes two good chapters. In spite of being comprehensively referenced the text is readable and there is little overlap between chapters written by experts from both sides of the Atlantic. There are sections on basic mechanisms such as 'kindling', the importance of the limbic system in epileptic disorders and the effects of psychotrophic drugs on the seizure threshold. The majority of chapters deal with clinical matters: the relationship between psychopathology and anti-epileptic drugs, the incidence of depression, which is relatively high, and its treatment in seizure patients, similarly psychosis.

There is an interesting section on the epidemiology and clinical aspects of the precipitation of seizures by anti-depressants, even where there is no previous history of epilepsy. Virtually all these drugs are incriminated, with nomifensine the least likely to offend. The use of anti-convulsants in psychiatric illness in the absence of epilepsy is reviewed at length, and theoretical implications discussed. It is, however, a pity that the difficult area of the inter-relations between epilepsy and hysteria are not covered.

In all a very useful book, and not merely for reference.

D. F. SCOTT, *Section of Neurological Sciences,*
The London Hospital

AMERICAN JOURNAL OF PSYCHIATRY

Volume 143, Number 1 January 1986

Special Article

1 An Etiologic Model of Alcoholism *James M. Donovan*

Regular Articles

12 Social Class and Psychiatric Practice: A Revision of the Hollingshead and Redlich Model *Richard F. Mollica and Mladen Milic*
18 Continuation Drug Therapy for Major Depressive Episodes: How Long Should It Be Maintained? *Robert F. Prien and David J. Kupfer*
24 The Persistent Risk of Chronicity in Recurrent Episodes of Nonbipolar Major Depressive Disorder: A Prospective Follow-Up *Martin B. Keller, Philip W. Lavori, John Rice, William Coryell, and Robert M. A. Hirschfeld*
29 Antidepressant Effects of Carbamazepine *Robert M. Post, Thomas W. Uhde, Peter P. Roy-Byrne and Russell T. Joffe*
35 The Overt Aggression Scale for the Objective Rating of Verbal and Physical Aggression *Stuart C. Yudofsky, Jonathan M. Silver, Wynn Jackson, Jean Endicott, and Daniel Williams*
40 Generalized Anxiety and Generalized Anxiety Disorder: Description and Reconceptualization *David H. Barlow, Edward B. Blanchard, James A. Vermilyea, Bonnie B. Vermilyea, and Peter A. DiNardo*
45 The Clouded Crystal Ball: A 35-Year Follow-Up of Psychiatrists' Predictions *C. Knight Aldrich*
50 Predictors of Shorter-, Medium-, and Longer-Term Outcome in Schizophrenia *Thomas H. McGlashan*
56 Family Environment as a Predictor of Psychiatric Rehospitalization *David Spiegel and Terry Wissler*

Editorial

61 A New Year's Appreciation *J. C. N.*

Brief Communications

68 "Can We Talk?" The Schizophrenic Patient in Psychotherapy *A Recovering Patient*
71 Autism and the Fragile X Syndrome *Gene S. Fisch, Ira L. Cohen, Enid G. Wolf, W. Ted Brown, Edmund C. Jenkins, and Anne Gross*
74 Family Violence and Child Adjustment: A Comparative Analysis of Girls' and Boys' Behavioral Symptoms *Peter Jaffe, David Wolfe, Susan Kaye Wilson, and Lydia Zak*
77 Influence of Factors Before and During Medical School on Choice of Psychiatry as a Specialty *George H. Zimny and Lindbergh S. Sata*
81 Prediction of Postdexamethasone Cortisol Levels by Serum Sodium Levels in Patients with Major Depression *Gary D. Tollefson, Janet Zander, Michael Luxenberg, Sanja Saxena, Michael Godes and Michael J. Garvey*
85 Combination Alprazolam-Neuroleptic Treatment of the Positive and Negative Symptoms of Schizophrenia *Owen M. Wolkowitz, David Pickar, Allen R. Doran, Alan Breier, Janyce Tarell, and Steven M. Paul*

Clinical and Research Reports

88 Pituitary-Adrenocortical Hyperfunction and Intolerance to Fluvoxamine, a Selective Serotonin Uptake Inhibitor *Walter Armin Brown, Mihaly Arato, and Ram Shrivastava*
90 Seasonal Major Affective Disorder *Peter A. Bick*
92 Case Report of Psychiatric Intervention by Mail: A Way of Responding to a Suicidal Crisis *Douglas Jacobs and John E. Mack*
94 Association Between Bipolar Affective Disorder and Multiple Sclerosis *Randolph B. Schiffer, N. Margaret Wineman and Lowell R. Weitkamp*
96 Ventricular Dilation on Cat Scans of Patients with Anorexia Nervosa *Steven Datlof, Paul D. Coleman, Gilbert B. Forbes and Richard E. Kreipe*
99 Melancholic Subtyping: A Qualitative or Quantitative Distinction? *Mark Zimmerman, William Coryell, and Bruce Pfohl*

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Index to Advertisers

Pharmaceuticals
The Boots Company plc .... *facing* p 158
CP Pharmaceuticals Limited .... *facing* p 186
Janssen Pharmaceutical Limited .... *facing* p 158
May & Baker Limited .... *facing* p 150
E. Merck Limited .... *facing* p 165
E. R. Squibb & Sons Limited .. *facing* p 151 and 159
Upjohn Limited .... *facing* p 164

Clinics, Hospitals and Nursing Homes
St. Andrew's Hospital .... p iii
The Retreat .... *inside back cover*

Booksellers and Publishers
Churchill Livingstone .... p v
Harvard University Press .... p iv
Methuen & Co. Limited .... p vi
Sweet & Maxwell Limited .... p iv
John Wiley & Sons Limited .... p iv

Appointments
University of Maryland .... p ii
University of Otago .... *facing* p 187

Miscellaneous
Mental Health Foundation .... *facing* p 187 and p ii
The Tavistock Clinic .... p ii

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THE BRITISH JOURNAL OF PSYCHIATRY

February 1986 Volume 148

Papers

The Northwick Park Study of First Episodes of Schizophrenia:

I. Presentation of the Illness and Problems Relating to Admission; *E. C. Johnstone, T. J. Crow, A. L. Johnson and J. F. MacMillan* 115

II. A Randomised Controlled Trial of Prophylactic Neuroleptic Treatment; *T. J. Crow, J. F. MacMillan, A. L. Johnson and E. C. Johnstone* 120

III. Short-term Outcome in Trial Entrants and Trial Eligible Patients; *J. F. MacMillan, T. J. Crow, A. L. Johnson and E. C. Johnstone* 128

IV. Expressed Emotion and Relapse; *J. F. MacMillan, A. Gold, T. J. Crow, A. L. Johnson and E. C. Johnstone* 133

The 'Italian Experience' Reconsidered; *Kathleen Jones and Alison Poletti* 144

The General Hospital Psychiatrist: Too Many Tasks and Too Few Roles? *Tom Sensky* 151

An Evaluation of a Time-limited Programme of Dynamic Group Psychotherapy; *Barbara M. Dick and Kate Wooff* 159

Parental Loss by Death in the Early Childhood of Depressed Patients and of their Healthy Siblings; *C. Perris, S. Holmgren, L. von Knorring and H. Perris* 165

Perceived Depriving Parental Rearing and Depression; *C. Perris, W. A. Arrindell, H. Perris, M. Eisemann, J. van der Ende and L. von Knorring* 170

Affective Disorder amongst Women in the General Population: A Longitudinal Study; *P. G. Surtees, S. P. Sashidharan and C. Dean* 176

Radio Receptor Assay of Serum Neuroleptic Levels in Psychiatric Patients; *Janet Krska, G. Sampath, A. Shah and S. D. Soni* 187

Hospital Doctors' Management of Psychological Problems; *Richard Mayou and E. B. O. Smith* 194

Conversion Without Hysteria: A Case Report and Review of the Literature; *Arieh Shalev and Hannan Munitz* 198

Effects of Intravenous and Subcutaneous Administration of Apomorphine on the Clinical Symptoms of Chronic Schizophrenics; *E. K. G. Syvalahti, E. Säkö, M. Scheinin, K. Pihlajamäki and J. Hietala* 204

Brief Reports

49, XXXXY Chromosome Anomaly: An Unusual Variant of Klinefelter's Syndrome; *T. Hari Singh and Sudhir Rajkowa* 209

49, XXXYY Chromosome Anomaly in a Mentally Retarded Man; *Valerie A. Cowie, K. Rameshwari Singh and Richard Wheater* 210

Koro–A Psychophysiological Dysfunction? *F. Oyebode, R. Jamieson, J. Mullaney and K. Davison* 212

Correspondence 215

Book Reviews 220

Notice to contributors, subscribers and advertisers inside front cover

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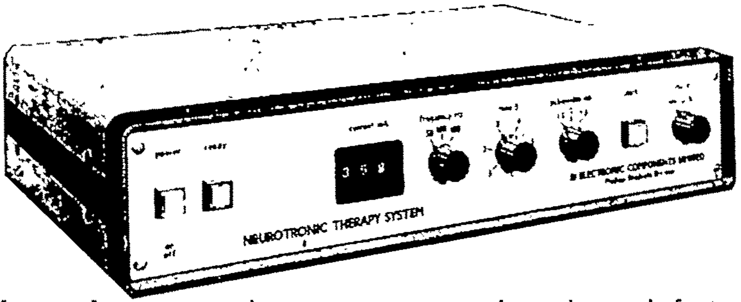

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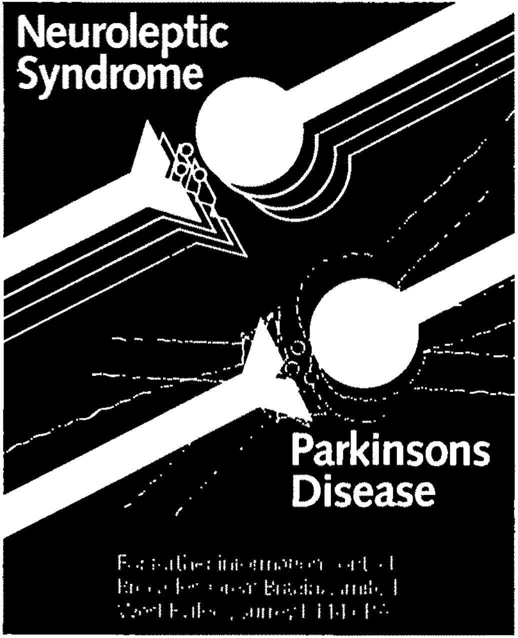

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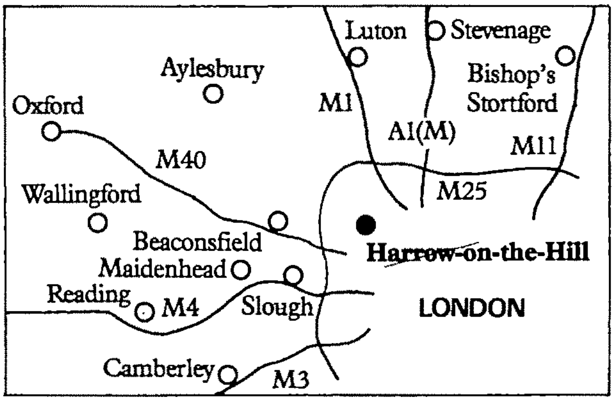

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British Journal of Psychiatry (1986), **148**, 227–234

Lecture

Socio-Psychiatric Aspects of the Young Severely Mentally Retarded and the Family

19th Blake Marsh Lecture delivered before the Royal College of Psychiatrists, February 1985

ANNALISE DUPONT

Interest in the different diagnostic groups of the mentally retarded started in the 19th century, but this made little contribution toward better treatment and care. Medical interest was mainly focused on the prevention of mental retardation. It was not until the 1950's and 60's that interest in research in the care and treatment of these persons intensified. The next step, study of the interaction between handicapped persons and the environment is the key to a better understanding of how to plan for work with the handicapped. New members of the therapeutic team (e.g., psychologists, and sociologists) will take over (Edgerton, 1984) if medical groups, especially psychiatrists, do not become more aware of the importance of the interaction between the handicapped and the environment.

It remains a puzzle how it is possible for one mentally retarded person to live peacefully in the family and attend a sheltered workshop without any difficulties, while another person—(perhaps with better intellectual function, but still in the severely handicapped group)—fails, either due to the demands of his work or of his family life. Discussions of the results of the modern community treatment of the mentally retarded also reveal specific problems (e.g., isolation of the adult living in the community; and the burden upon the caretaker, often the mother of a mentally retarded person living at home).

For many years psychiatrists working with the handicapped were forced to work with large groups (e.g., in large mental hospitals) and therefore the disabilities and problems of the individual person and family were difficult to describe. The study of this process has been accelerated by the changing sociological patterns in mental handicap (Primrose, 1984). There are also new trends: major demographic changes, according to birth rate; age distribution of mothers; higher survival rates of the more severely mentally handicapped; and changes in the different aetiological factors and complications among the surviving mentally retarded.

If we want to study the life of the mentally retarded, it is necessary to describe in detail: (1) the individual's functioning and his or her impairments, disabilities and handicaps (World Health Organization (WHO, 1980); and (2) the impact on the environment of the handicapped person's characteristics.

Description of the person

It is often repeated that an uncomplicated case of severe mental retardation is very rare, so description is incomplete unless all additional diagnoses and their degrees are added: the more severe the intellectual handicap, the more additional handicaps. These disabilities are caused by: (i) the pathology of mental retardation, for instance a chromosomal abnormality causing congenital abnormalities; (ii) brain damage or brain dysfunction connected with mental retardation also causing epilepsy; (iii) other diseases, not included in the above mentioned groups, but related to the patients' condition, their general weakness, their abnormal immune-biological system, and their abnormal life situation; (iv) psychosomatic or psychiatric diseases, for instance behaviour abnormalities and neuroses; and (v) interaction of more than one syndrome in one patient, e.g., Down's syndrome and hypothyroidism, or mucopolysaccharidosis and a chromosomal abnormality.

For all the above mentioned different additional diagnoses there are questions of degree, for instance of epilepsy, and of the nature of the interaction of the additional disabilities with mental retardation.

However, even in the WHO system (1980) it is difficult to classify each individual's multiple handicaps as a new complex.

Description of the impact on the environment

This depends upon the background of the professionals. Psychologists may use the method of ecology as defined by Cambell (1981). The Swedish psychologist Kylén (1974) analysed "the general framing of the question regarding the conditions for the interaction between mentally retarded and their milieu". In addition, the sociological method used in surveys of the family and the handicapped child has been very useful (Wilkin, 1979).

Caring for the mentally retarded in developing countries

Sell (1984) has discussed services for the mentally retarded person and his family in developing countries and the special challenge of planning. He highlights two reasons for difficulties: first, the tendency for there to be no clear responsibility for service activities on the part of departments or agencies. In many developing countries health agencies do offer some services for the retarded. Departments of education and social welfare departments are also involved. Policy documents on mental retardation stress the importance of preventive measures, most of which are outside the scope of activities of the agencies engaged in work with the retarded. The second reason for difficulty in planning for the mentally retarded is the frequent absence of clear aims. Sell (1984) stresses that one of the most important needs of the mentally retarded is their right to survival. Another area in which data would be needed within the context of a study of needs concerns coping mechanisms within families and the objective and subjective burden placed on families by the presence of a retarded person. Here we are faced with a new pattern of ecology, and, for example, the system of joint families in developing countries is said to provide a network of support for handicapped and impaired persons; whereas, in fact, existing data appear to invalidate such belief (Mia *et al,* 1979; Gupta & Sethi, 1970). Sell's (1984) conclusions are the following: mentally retarded persons may have a very short life expectancy in certain social strata of some developing countries, and the presence of a retarded child or adult in the family may pose a serious threat to the cohesion of extended families, especially in rural societies.

The family of the mentally retarded youngster

The most important unit involved with the handicapped person in childhood and adolescence is the family. A description of the different types of families could either describe mentally retarded without other handicapping conditions (Crnic *et al,* 1983) or analyse all cases from an epidemiological study (Dupont, 1980). If the person is only disabled according to impairment of intellect, and the additional symptoms are excluded, it is a limited task to deal with problems of stress, coping, etc. However, even a book on normal families (Olson & McCubbin, 1983) which examines over 1000 intact families at all stages of the life cycle has difficulty in conveying which qualities help families to deal with stress and problems across the life cycle. Very complicated methods are used in order to describe the problems of the family members, and how families who cope differ from those which have difficulties. Therefore, it is not surprising that it has not been possible to describe in detail the function of a family with a multiple handicapped mentally retarded member.

A recent publication from Norway by Ingstad & Sommerschild (1983) dealt with families with a handicapped child (not only with mental retardation, but also children with other chronic diseases). They described the large variations in how a family reacted. Some families eventually found a way of coping and compensating both for the extra demands of the handicapped and for the needs of the other family members. Other families, however, were not able to find a solution of their own, and so depended on outside help. Analyses of qualitative data showed how the past created important constraints and possibilities for coping in the present situation. For those who represented the strongest and the weakest forms of coping, it was possible to identify "good" and "bad" coping styles. Many other family life style studies have been performed (e.g., Graliker *et al,* 1962; Gath, 1972, 1973; Bayley, 1973; Friedrich, 1979; Blacher & Meyers, 1983; Beckmann, 1983; Nihira *et al,* 1981, 1983).

Mink *et al.* (1983, 1984) studied two groups: (i) homes with trainable mentally retarded (TMR) children (Mink *et al,* 1983); and (ii) homes with slow learning children (SLC) (Mink *et al,* 1984). In both studies a battery of instruments dealing with family social environment and family and child characteristics and behaviour was administered to groups of families. A cluster-analysis was performed on the different variables. In both studies it was possible to identify unique family clusters, and also to profile similarity of cluster '1' in the TMR taxonomy study with cluster 'A' of the SLC study. They indicated that there may be homology in family types regardless of the degree of retardation of the child. The authors were also able to compare the identified parent/child interaction with earlier published models (Vietze & Anderson, 1981). However, these family clusters were described without regard to the additional handicaps of the child.

Wilkin (1979) examined the homes of 120 mentally retarded children in age groups ranging from 0–16 years. He found a surprisingly low relationship between social class and whether or not the family was seeking long-term care. From a sociological point of view, he studied (more thoroughly than other authors) the role of the sexes in the care-taking work of families. In one of his chapters, he concluded that "community care does not mean care by the community, nor does it mean care by the family, it means maternal care with varying but generally low levels of support from others". In most cases mothers carried the burden of child care and house work with little support from their families, relatives, friends and neighbours, and in general the health services had little obvious direct impact on the problems of day care of the majority of handicapped children.

Investigation of the family and the young mentally retarded in the age group 13–21

Method

Based upon an epidemiological study (Bernsen, 1976) of severe mental retardation in the county of Aarhus, Denmark, a study was performed in 1977 on the 39 families with a child between 6 and 14 years (Dupont, 1980); all the children were living at home and attending day institutions or schools (with one exception). In 1984 *the present follow-up study* was performed with visits by the author to all the families. The computer files from 1977 were still available, and data from the first survey could be compared with data produced in 1984. A schedule with the same questions as in 1977 concerning the time spent by the care-taking parent(s) was worked out for each minute, and produced for a week by each family.

As a basis for a questionnaire, the same lists of disabilities were used: mentally retarded with delayed motor development; feeding problems; not toilet trained; passive; hyperactive; cannot be brought by public transport; hard of hearing; visually handicapped; epileptic; cerebral palsy; skin disease; weight problems; special teeth problems; special problems with supervision (babysitter); financial problems; and problems with siblings. For each group of problems the need for technical aid(s) and/or materials and the need for care-taking personnel and time was listed. According to the lists, a weighting of 1–3 for disabilities and variables concerning burden was given to each of the youngsters. The youngsters were grouped according to degree of burden, in groups 1–4. The rating was computed using the same Handicap. Behaviour and Skills Schedule (HBS) as used by Bernsen (1981) and described by Wing & Gould (1978). As the benefits of relief stays, short-term, long-term, regularly or according to sudden needs, are important for families, questions were asked in this regard: how often, how, and where is it arranged? Day institutions, leisure activities, special courses and the future plans for the youngsters, and the parents' employment and other living conditions were included in the analysis. Fig. 1 shows the population of the area, the municipality of Aarhus with 250 404 persons.

Results

Table I shows the changes from 1977 to 1984. The original sample was 39, and in 1984 this was reduced to 29 (18 men and 11 women) as five children had died and five had entered a mental retardation institution. The most severely handicapped group was group 1. These five youngsters were totally non-mobile and in need of help for all daily activities; often multiple handicapped (e.g., with epilepsy); language and social communication was absent or severely impaired; they were prone to infections; and had disturbed sleep patterns. Group 2 comprised 11 youngsters who were typically hyperactive; destructive; non-communicating or passive; and were in need of much help. Often they had sense and language impairment, or other handicaps. Some of them had repetitive routines or other behaviour problems. Group 3 consisted of seven youngsters who were

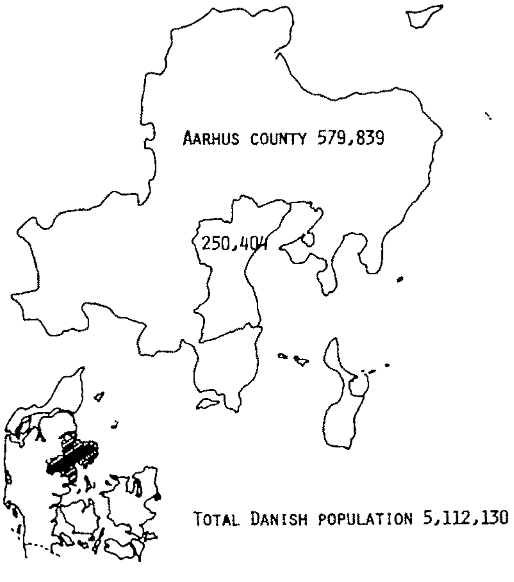

FIG. 1. The population of the described area 1.1.1984.

TABLE I

Number of handicapped adolescents—group distribution according to severity of symptoms (Group 1: the very severely-handicapped; 4: the least handicapped group)—and number of dead and institutionalised

Group 77 \ Group 84	1	2	3	4	Total in 1984	Dead in 1984	Now living in M.R. institution	Total in 1977
1	4	0	0	0	4	5	1	10
2	1	10	4	0	15	0	2	17
3	0	1	3	3	7	0	2	9
4	0	0	0	3	3	0	0	3
Number of mentally retarded persons	5	11	7	6	29	5	5	39

TABLE II

Handicapped adolescents—variables for burden and number of youngsters

Variable	Weight	Number of youngsters
Cannot walk	3	7
Fits (grand mal and other types)	3	12
Not toilet trained	3	15
Must be spoon-fed	3	12
Tears clothes	3	12
Hyperkinetic, with self-mutilation and other abnormal behaviour	3	5
Destructive and/or aggressive	3	9
No understanding of danger (for instance in traffic)	3	18
Blind or severely visually impaired	3	5
Cerebral palsy	3	11
Permanent supervision necessary	3	21
Disturbs parent's sleep	3	14
Messing with food	2	17
Drivels, spits, ruminates or the like	2	15
Too difficult in public transport	2	21
Insufficient or no communication	2	20
On medicine	1	11
Passive	1	23
Uses glasses	1	6
Skin disease or sensitive skin	1	11
Need of special dental care	1	27

TABLE III

Handicapped adolescents—Age of mother-groups in 1984

Age, years \ Group:	1	2	3	4	Total
No mother	0	1	0	0	1
30–39	0	4	0	0	4
40–49	5	2	3	4	14
50–59	0	3	2	2	7
60–69	0	1	2	0	3
Total	5	11	7	6	29

TABLE IV

Handicapped adolescents—Age of father-groups in 1984

Age, years \ Group:	1	2	3	4	Total
No father	0	2	3	1	6
30–39	0	3	0	0	3
40–49	5	4	3	3	15
50–59	0	1	1	2	4
60–69	0	1	0	0	1
Total	5	11	7	6	29

mobile; not toilet trained at night; often had epilepsy or other handicaps (of mild degrees); and needed some help with daily activities. Group 4 contained six youngsters who managed daily life routines; and had social interaction and skills corresponding to those of the normal person at a chronologically lower age. It is notable that all the children who had died belonged to the heavy loaded group in 1977, but the children now living in institutions showed great variations as is shown in the Table. The most important factors in the decision to send the child to an institution were changes in family status: e.g., the father died or was divorced, or the lonely mother remarried. In all the other 29 families the family pattern was very stable. However, in 1984 one family showed a new pattern: the father was divorced, living with and caring full-time for his mentally retarded youngster.

Table II shows the weight ratings and the number of youngsters with each disability. If the results are analysed for the two age groups 13–17 and 18–21, there is a tendency towards higher weight ratings for the younger age group, but no significant differences.

Tables III and IV show the age of mothers and fathers (average age of fathers: 46 years, of mothers: 47 years). In

TABLE V
Handicapped adolescents—Average time spent with the youngster in hours per day

	Monday	Tueday	Wednesday	Thursday	Friday	Saturday	Sunday	Weekdays	Weekends	Mean
At night	14	23	16	13	18	28	13	17	21	18
Bedtime	14	14	12	12	11	17	17	13	17	14
Care	73	70	72	76	77	75	89	74	82	76
Dressing and maintenance of clothes	47	48	51	51	49	53	44	49	48	49
Preparation of food and feeding	65	58	65	58	66	77	81	63	79	67
Occupation	71	70	73	74	74	116	123	72	119	86
Miscellaneous	91	111	88	129	107	103	91	105	97	103
Total (min)	375	394	377	413	402	469	458	393	463	413
Total hours and minutes	6 h 15 m	6 h 34 m	6 h 17 m	6 h 53 m	6 h 42 m	7 h 49 m	7 h 38 m	6 h 33 m	7 h 43 m	6 h 53 m

TABLE VI
Handicapped adolescents—Average time spent daily with 29 youngsters in the four groups

Number of youngsters	5 Group 1		11 Group 2		7 Group 3		6 Group 4	
Weight load	26–38		15–38		6–29		1–10	
	Hours	Minutes	Hours	Minutes	Hours	Minutes	Hours	Minutes
Night	0	11	0	35	0	03	0	04
Bedtime	0	27	0	10	0	03	0	23
Care	1	20	1	19	0	54	1	37
Clothes	0	41	0	53	0	37	1	08
Food	1	33	0	58	1	16	0	39
Occupation	1	06	1	40	1	00	1	58
Miscellaneous	1	23	2	02	1	52	1	05
Total	6	41	7	37	5	45	6	54

six cases the mother was alone with a youngster (all men); and in one case the father was alone with a young boy—in this family there were two children, both severely mentally retarded, and after divorce each parent had one child. In three families there were two parents, but one father was too old to take part in care, another was too ill, and the third was not interested (the mentally retarded child was not his biological child). In another five families, each with both biological parents, the father performed a great deal of the work.

Parental employment

Of the 19 cases where the mother performed nearly all the work, the mother was ill in five cases (one with diabetes, one with severe rheumatism, and in the other cases there were back problems and other consequences of the heavy burden). In 14 cases the mother was at home full-time, in three cases the mother was working full-time outside the home, and in five cases the mother had part-time work outside the home. There was a tendency to increase the number of working hours up to full-time if the work of caring for the severely mentally retarded child did not preclude it. Two of the mothers without work outside the home took part in the firm which the father had established in the family home. One of the mothers expressed deep sorrow that she had never been able to continue the work she had been trained for. The father caring full-time alone with a severely mentally retarded youngster was unemployed and had no intention of trying to work outside home because it was impossible with the responsibility of the severely handicapped boy. In one family the mother had a training which would have enabled her to obtain highly qualified work outside the home, and during the last few years she had taken some part-time work in the evenings.

Table V shows the average time spent by the parents with their handicapped youngsters (for the whole group), and Table VI shows this for each of the four groups of severity of symptoms. The highest figures for time spent with the youngsters are due to activities related to care-taking (care, dressing, feeding, etc.), and occupation and training accounted for less time. The "miscellaneous" category included, in particular, mending and washing clothes. The average time spent on each youngster varied from 1–12 hours. All the youngsters attended some sort of school or sheltered workshops. Leisure activities and courses were arranged for two-thirds of them (the less severe cases) and included taxi transportation (except in two cases).

Results of the comparison with the 1977 study

When the child's handicap was severe and complicated, the impact on the daily life of the family was also very severe. The time spent on the daily care of the handicapped family member was nearly the same for the two age groups. The small decrease in time for the youngster group was mainly caused by a decline in the average time for occupation and training (from an average of two hours and 14 minutes to one hour and 26 minutes). The psychological aspects of improvement were disappointing in 22 cases; although the professionals and the parents have worked very hard with training of the youngsters, and have consulted and discussed with experts, the results were poor.

The grouping according to disabilities showed that 20 were in the same group, two were more severely handicapped, and seven went to a less severe group (from group 2 to group 3). Two of the well-functioning girls from the best group (both with Down's syndrome) could well be classified as mildly mentally retarded, although in 1977 they belonged to the group with an IQ below 50. The parents indicated clearly that the girls' development had been very satisfactory. In some cases medical difficulties increased, e.g., due to progression of epilepsy, cerebral palsy and other additional handicaps. With regard to communication and development of language and speech, in half the cases the parents considered that they were better able to understand their child's wishes, and that it was more possible to attend to all their needs and demands.

According to the results from the computerised files, the sleep pattern of the more severely handicapped was less abnormal in 1984 than in 1977. Five of these cases were of Down's syndrome. The two women will probably be able to live in a hostel and work in a sheltered workshop. But all three men are developing very badly and are so aggressive that it is questionable when the mother will have to give up. In all three cases the mother is working alone because the father is too old. In one case where the mother is 59 years old, and in another case where the mother is chronically ill (rheumatic illness), the father left home many years previously. The third Down's syndrome youngster is not only handicapped by his syndrome, but also has brain damage following an accident in which he nearly drowned and was unconscious for a long period. His mother is also alone (divorced).

Puberty was associated with some changes. Among the women, the menses caused no problems or only slight problems in seven cases, but in four cases there was severe or moderate menstrual dysphoria. Of the 18 men, four had severe epilepsy, and in three cases grand mal fits had become worse. In one case, however, all fits had disappeared. In two cases with cerebral palsy there were no changes. In nine cases masturbation was a severe or moderate problem. In two cases of grown-up mentally retarded boys, interest in touching and examining women prevented them visiting public places.

In 1977 the families' main complaints concerned *the need for supervision*, in many cases all day and night. Of the 39 children, 21 had to be supervised constantly or could only be left alone for a few minutes. The same situation was found in 21 of the 29 cases in 1984. A new pattern was that five of the youngsters were now able to stay at home alone for hours; in some cases the parents had taught the youngsters how to telephone them when they were out. In some cases there were other arrangements, but the supervision burden in these cases was less severe. However, for severely handicapped youngsters it was found that 17 cases needed more supervision in 1984 than they did earlier (the number in the group in which the child could be left alone for about half an hour had decreased). This meant that parents were not able to leave home for a short visit, e.g., to go to the supermarket. According to the parents alteration was mainly due to the increase in the children's physical strength without better social adaptation, which meant that the youngsters were able to open windows or doors, or to evade security arrangements. It was also related to the high degree of destruction and aggressiveness which some of the youngsters showed periodically.

The results of the first paper on burden were published widely in Danish periodicals for administrators and other professional groups. The findings were also useful to the parents' organisation. Socialforskningsinstituttet—the Danish National Institute of Social Research—published a paper one year later on the need for arrangements for relief and leisure in families with mildly and severely handicapped living at home (Pruzan & Spohr, 1981). In our follow-up study it was obvious that the relief situation had improved; arrangements for families followed a new pattern: one day a week, and one week-end per month the family received payment for and had the opportunity to let the child stay overnight in a day and night short-term institution. A few cases (the most severely handicapped) were sent to more hospital-like institutions. Only one family was offered this arrangement and failed to take it up (the child was very severely retarded and had cerebral palsy). In nearly all cases siblings had left home, and grandparents were now dead or unable to assist the parents.

Discussion

For decades the usual pattern for a family with a severely handicapped child has been for them to adapt to the needs of the handicapped family member. Many studies have described the situation during childhood. However, nearly all the cases now stay at home during adolescence, and few follow-up studies have been performed over this period. The age group 13–21 is difficult. In the present study, the average age was 17.2 years. The young person was pubertal or post-pubertal and was, in effect, grown-up. As one of the mothers expressed it: "One moment I am helping my grown-up son to shave, and the next moment I am changing his nappy." The alternative to staying at home for this group is sheltered accommodation, hostels, small group-arrangements or the like. For the most severely handicapped the alternative is an institution for the mentally retarded. Only for one of the 29 (a Down's syndrome woman) was a group-residence with other youngsters considered.

The families' ability to cope with the problems varied a great deal. This was not always related to family structure—in some cases a mother living alone with a severely mentally retarded youngster had fully adapted to the situation. For instance, the divorced mother of David: despite her very isolated and difficult life with her son (who had difficulties in walking and was unable to accompany her into a shop because of his tendency to lift ladies' skirts, touch people or to put his hands into everyone's pockets), this mother was able to say: "David and I have a wonderful life!"

Wikler *et al* (1981) described certain critical periods of family life with a mentally retarded child: the times of the normal milestones for walking, talking, starting school, puberty and work. Another factor is the age of the care-taking parent: in this study it is obvious that with increasing parental age there are increasing problems. For many families, in a few years the situation will become hopeless and another placement of the young person will be necessary. In two of the families with severe cerebral palsy children respiration is a growing problem, day and night, and is treated with a special valve (as a substitute for earlier treatment by a physiotherapist). One mother expressed her feelings towards work with the child thus: "At my age (49), all my friends and acquaintances have long passed the phases of toilet training their children, having disturbed sleep at night, and facing difficulties during shopping with a child who has soiled everything with faeces or vomit. That is why I find it so difficult to cope." In another family the father said: "I am still trying to finish my postgraduate training. All my contemporaries passed that stage many years ago, but I continue, and I hope that although I make very slow progress, I will succeed. All my spare time is used in looking after my severely handicapped son."

Although relief arrangements were established, parents complained that if the child became ill during short-term stays, the child was referred immediately to the hospital paediatric or neurological department. And soiled clothes always returned home with the child. As the short-term stay arrangement was not provided at the level of demand, the system was very rigid and inflexible to the needs of the parents.

When the youngster was ill, or the care-taking parent in families with one parent was absent, or where only one parent was able to look after the youngster, in some cases it was impossible to provide relief arrangements. According to the responsible authorities, there was the possibility of a municipality home-visiting aid, but in cases where the youngster was aggressive, the available aids refused to come. A desperate mother said that she was forced to take her ill, severely mentally handicapped, not toilet trained, boy to her shop for the whole day. There was a small room behind the shop where she secured him to a bed. Many of the care-taking parents stressed that it was possible to adapt the handicapped youngster to daily routine without great difficulties, but as soon as this quiet and stable routine was broken, everything went wrong.

Both our first study and this follow-up investigation show the significance of additional handicaps, of all types and degrees, and the problems they cause. Conditions for handicapped persons in this part of the country and for this age group have developed in the same way as those in other counties and other age groups. Where there are differences, the service in this county is better, and the younger age groups have been given more attention and care than the older ones.

How many families are involved? In 1978 an analysis of the nationwide register of all 7600 mentally retarded aged 17 years or more was performed. This showed that 4800 or 63% of those registered lived with parents or close relatives (2/1000 of all Danish families).

For many years institutional treatment blocked the development of the medical specialty of oligophrenia or oligophrenology. Today it is natural to classify it as a sub-group of social psychiatry which is a young and fast growing field (Freeman 1984). The social psychiatrist is welcome in the team and is able to participate in the work on many different levels not only in the daily treatment but also in the development of social psychiatric research. Techniques of service evaluation (Judd & Kenny, 1981), the advanced statistical treatment of data, and improved methods of questionnaire design and attitude measurement (Oppenheim, 1966) have recently created more respect for social psychiatry; more especially since the coming of logit analysis, cluster analysis, and the like. Analysis of a fraction of the ecology of the handicapped mentally retarded, which has started with their family and relations, could be developed to include many other aspects of their life.

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Annalise Dupont, MD, PhD., Lecturer, *Aarhus University, Head of Institute of Psychiatric Demography, Psychiatric Hospital, DK-8240 Risskov, Denmark.*

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Review Article

Volatile Substance Abuse: A Review of Possible Long-Term Neurological, Intellectual and Psychiatric Sequelae

MARIA A. RON

The possibility that chronic abuse of volatile substances can cause permanent neurological, psychiatric, and intellectual sequelae is critically reviewed. Toluene, present in the commonly used adhesives, is most often implicated in 'glue sniffing'; this review focuses on its potential long-term effects. Many criticisms—particularly poor matching of control samples and inability to distinguish between acute and chronic effects—can be levelled at the available studies, while no adequate follow-up studies have been performed. In the light of present knowledge, the possibility that permanent structural brain damage, with accompanying psychiatric manifestations, results from solvent abuse remains inconclusive.

The abuse of volatile substances (VS) has been identified as a problem in the USA for more than 20 years (Merry & Zachariadis, 1962). By the mid-1960s, the practice appears to have been widespread there, and by 1970, the first cases had been recognised in Scotland (Watson, 1982). Since then, the problem has caused considerable public concern and has received extensive media coverage. Among the many chemicals that have been abused, toluene—contained in commonly used adhesives—has been the main substance involved in 'glue sniffing'; its effects have certainly been described more often than those of other solvents. However, while the acute effects on the central nervous system are well known, the possibility that long-term neurological and psychiatric sequelae could result from the practice has not been systematically explored.

This review attempts a critical evaluation of the possible long-term effects of solvent abuse, paying special attention to those of toluene. The acute effects and other epidemiological, social, and medical issues are considered only when they appear relevant in understanding the possible permanent effects.

The Size of the Problem

In America, where the problem has existed for much longer, Fishburn *et al* (1980) studied a mixed urban and rural population, stratified for age, and reported a life-time prevalence of 16.5% for subjects aged 12 to 17. Only 2% of that age-group had abused VS in the preceding month, and in most instances the practice had been sporadic. The prevalence rates were lower for older subjects (9.8% for those aged 18 to 25 and 3.9% for those older than 25). Similar figures have been reported by Sharp & Korman (1981).

In the UK, the prevalence of VS abuse is still uncertain, the available information referring to groups which may not be representative of the general population while under-reporting in school surveys may give erroneous prevalence figures. Ramsey (1982) found a point-prevalence of 9.8% for boys aged 13 to 15 attending a Glasgow secondary school: one quarter of them reported using VS regularly, another quarter sporadically, the rest only once, and no abuse was reported by those aged 16 or over. As can be expected, the figures are lower when only those who come to the attention of different agencies are considered. Thus, in the county of Avon, Gay *et al* (1982) identified 304 abusers from a population of 250,000 individuals at risk during a six-month period; 77% were aged between 14 and 17. In this sample, only 24% had abused solvents for more than six months, and only 4% had also abused other drugs or alcohol.

Abuse of VS as the presenting problem or as a contributory factor accounted for 3.5% of all referrals below the age of 16 to the Department of Child Psychiatry at the Maudsley Hospital (Skuse & Burrell, 1982) and for 1% of all requests for information received by the National Poisons Information Service (Francis *et al*, 1982). In the UK, as in America, VS abuse appears to be at least twice as common in males as in females. Finally, 140 fatalities related to this practice were reported in the UK between 1971 and 1981 (Anderson *et al*, 1982); the 39 that occurred during 1981 accounted for 1% of all deaths in the age-group 10 to 19, and for nearly 2% of deaths due to injury and poisoning in the same age-group.

This information does not allow us to draw firm conclusions about the extent of the problem. Nevertheless, it would appear from the results of point-prevalence studies that only a minority of those who experiment with these substances go on to use them regularly, and that so far, the problem is largely confined to those under the age of 16, although this pattern may change in future. The possibility that solvent abuse could escalate into a progressive career of addiction is of considerable importance. So far, only anecdotal reports of such cases have been published (Merry, 1967). Davies *et al* (1985) recently described four cases of solvent abusers from deprived socio-cultural backgrounds who later became heroin addicts, but whether this trend is commoner than hitherto supposed remains to be ascertained.

The Substances Abused

A variety of volatile substances have been used to produce altered states of consciousness (Table I).

TABLE I
The Substances Abused

Toluene		Adhesives
Acetone		
n-Hexane		
Ethyl acetate		
Methyl ethyl ketone (MEK)		
Methyl butyl ketone (MBK)		
FC 11	(Freons)	Aerosols
FC 12		
Methylene chloride		
Isobutane		
Propane		
Chloroform		Solvents
Trichloroethylene		
Carbon tetrachloride		
Trichloroethane		
FC 113 (Freons)		
n-Hexane		
Carbon tetrachloride		Fire extinguishers
FC 13 B1		
BCF	(Freons)	
FC 114 B2		

(From Clark & Tinston, 1982)

Surveys in the UK (Watson, 1982; Sourindhrin & Baird, 1984) have shown that nearly 90% of abusers used adhesives containing toluene and acetone; dry cleaning fluids containing toluene, trichloroethylene, and carbon tetrachloride were used by only 5%, butane by 3%, and other products such as nail polish remover, hair lacquer, and fire extinguisher fluids by less than 3%. These declared preferences have been confirmed by analysis of blood and urine samples during acute intoxication. Oliver & Watson (1977) detected toluene and acetone in 84% of 42 consecutive cases, and Francis *et al* (1982) found toluene in 73% of the samples received at the National Poisons Information Service. Trichloroethane and trichloroethylene were present in one-fifth of these cases, alcohol in 10%, and other drugs (mainly benzodiazepines) in 18%.

The pattern of VS abuse associated with fatalities is different, however. Anderson *et al* (1982) found that 71% of deaths directly attributable to VS abuse had been caused by aerosols, and less than one-quarter by toluene-containing adhesives. Similar findings have been reported by Watson (1979) and by Garriott & Petty (1980), while "sudden sniffing deaths" caused by aerosol inhalation combined with brief, vigorous exercise such as running have been reported by Bass (1970). The cause of death is thought to be cardiac arrhythmia, resulting from the action of catecholamines released during exercise on a myocardium sensitised by the freons used as aerosol propellants.

The effects

Toluene is a lipophilic aromatic hydrocarbon, derived from benzene; it has poor solubility in water, but is soluble in other solvents such as acetone, alcohol, and chloroform. Inhalation is the fastest method of incorporating toluene into the body tissues: if the concentration of toluene in the inhaled air remains constant, the blood concentration reaches 60% of its maximum after 10 to 15 minutes of exposure, and an asymptotic blood concentration curve is reached within half an hour. The concentration in richly vascularised organs such as the brain rises at a similar rate to that in the blood, although the former concentrations are at least four times greater. Although some toluene is eliminated unchanged through the lungs, most of it is oxidised to benzoic acid and, by conjugation with glycine, is converted into water-soluble hippuric acid, which is eliminated through the kidneys. During constant exposure to toluene, hippuric acid levels in urine reach 60% of their maximum after 40 to 60 minutes, and the elimination curve becomes asymptotic in two or three hours. Toluene cannot be detected in blood four to six hours after the cessation of exposure, by which time the concentration of hippuric acid in urine has decreased to 30% of its maximum value. A second peak in blood toluene, representing the release of lipid-bound toluene, has been described as occurring days after the cessation of exposure (King *et al*, 1981).

For toluene, the threshold limit value (TLV) or airborne concentration to which industrial workers can be repeatedly exposed without adverse effects is 100 ppm (parts per million). Toluene abusers are exposed to concentrations approximately 50 times greater, although the duration of the exposure is usually shorter.

Acute effects

The methods of inhalation of solvents vary depending on the product employed, but they all involve deep breathing through the nose or the mouth, often using strategies to maximise the concentration of solvent in the inhaled air. Glue is usually poured into a plastic bag, which is placed over the nose and mouth, or covering the whole head; other products such as dry cleaning substances are often inhaled directly from their containers or from impregnated rags, while aerosol contents are sometimes sprayed directly inside the mouth. Tell-tale signs of solvent abuse such as the characteristic smell on the breath, glue on the hands and clothes, and the glue sniffer's facial rash are well recognised (Watson, 1982). The social settings in which this practice takes place have also been repeatedly reported: in about two-thirds of all cases, solvent abuse is a group activity, but solitary abuse tends to occur in those with greater social and psychological problems (Gay *et al*, 1982).

Toluene, like alcohol and other volatile substances, exerts an excitatory effect on the central nervous system, followed by a depressive phase. The initial subjective effects are feelings of euphoria, disinhibition, exhilaration, tinnitus, dizziness, and difficulty in focusing. To the observer, the subject shows lack of coordination, slurred speech and impaired judgement, followed by lethargy and increased somnolence. These effects last for 30 to 45 minutes after cessation of exposure, and some degree of amnesia for the event is usual on recovery. Other features of acute intoxication include sneezing and coughing, nausea and vomiting, diarrhoea, diffuse pains, tremor, paraesthesia, and epileptic fits. Visual and, less commonly, auditory hallucinations have been reported in a variable proportion of subjects (King, 1982; Sourindhrin & Baird, 1984).

Blood levels of toluene are related to the severity of the clinical symptoms (Lush *et al*, 1980). Thus, concentrations of between 1 and 2.5 μg are accompanied by marked intoxication, those between 2.5 and 10 μg by greater disturbance of consciousness (often requiring hospital admission), and those at higher levels result in coma and possibly death. Compared with alcohol, toluene produces quicker and briefer intoxication and more perceptual distortions.

Increased tolerance to toluene has been reported after regular abuse for periods as short as three months (Glaser & Massengale, 1962; Press & Done, 1967; Hofmann & Hofmann, 1975). Withdrawal symptoms were not observed in a sample of out-patient abusers (Sourindhrin & Baird, 1984), although they have been described in a few severe cases admitted to hospital (Press & Done, 1967; Tsushima & Scott Towne, 1977; Watson, 1979; Lewis *et al*, 1981). The symptoms were similar to those of alcohol withdrawal, and were relieved by further use of the substance; in one case, a syndrome akin to delirium tremens has also been reported (Merry & Zachariades, 1962).

Only a minority of abusers with particularly severe and persistent symptoms require admission to hospital; in such cases, neurological impairment is the rule. Thus, in a group of 20 consecutive admissions reported by King (1982), coma was the presenting feature in five of them, epileptic convulsions in three, dysarthria in five, and ataxia in the rest. These findings are in agreement with those of Francis *et al* (1982) from the National Poisons Information Service, who received requests for information on 105 patients admitted to different hospitals in the UK. Impairment of consciousness appears to be quickly reversible in most cases (Streicher *et al*, 1981; King, 1982), and only 19% of the 105 admissions reported by Francis *et al* (1982) remained in hospital for more than 24 hours. This suggests that severe intoxication, rather than persistent structural damage to the brain, is the cause of these abnormalities.

Of the deaths reported in connection with VS abuse, the coroners' reports attributed half of them to accidents during intoxication (Anderson *et al*, 1982) and the rest to the direct effects of the chemical. However, most of these deaths were thought to be due to the cardiac effects of the solvents, and perhaps as few as 2% of them to the effects of solvents on the central nervous system.

Thus, there are considerable similarities between the acute effects of toluene and those of alcohol, and only a minority of abusers require hospital admission during the acute stages of intoxication.

Neurological symptoms are usually present in those who come to medical attention, but in the majority, these are quickly reversible and are likely to be due to transient rather than permanent brain changes. It seems therefore unjustified to subsume these abnormalities under the term 'encephalopathy' (King, 1982); individual analysis of the transient and persistent effects is more likely to prove fruitful.

The persistent effects

(a) *Cerebellar syndrome*

Persistent cerebellar signs have been reported in some cases of toluene abuse, but their incidence is not known. Grabski (1961) first described the syndrome in a patient who had inhaled toluene regularly and gasoline occasionally, for two years. Nystagmus, titubating gait, ataxia, and tremor in the limbs were the main symptoms; at follow-up, these symptoms had transiently improved during periods of abstinence. When his condition was reported again (Knox & Nelson, 1966), cerebellar signs were still present, but the picture had been complicated by carbon tetrachloride abuse. The same applies to other cases in which drug and alcohol abuse (Kelly, 1975; Lewis *et al,* 1981) or the presence of n-hexane in the mixtures inhaled (Escobar & Aruffo, 1980) may have played a part. However, others have described cerebellar signs in pure toluene abusers (Boor & Hurtig, 1977; Keane, 1978; Sasa *et al,* 1978; Malm & Lying Tunell, 1980; King, 1982; Ehyai & Freemon, 1983), and there is little doubt that this chemical alone can cause the syndrome.

The largest series of toluene-related cerebellar signs has been reported by Fornazzari *et al* (1983), who found them in 11 out of 24 toluene abusers admitted to a Canadian drug treatment unit. The presence and severity of the cerebellar signs were significantly correlated with the width of cerebellar sulci and superior cerebellar cisterns in the CT scan. The high frequency of cerebellar abnormalities in this series is likely to be related to the age of the subjects (mean age 23) and to the more severe and prolonged abuse, compared with previous reports. The natural history of the cerebellar abnormalities is still uncertain and, while recovery or considerable improvement takes place in some cases after weeks or months of abstinence, in that reported by King *et al* (1981), signs were still present 18 months later. Our knowledge of the neuropathological lesions responsible for the clinical picture is equally limited. In the only available post-mortem study, Escobar & Aruffo (1980) described loss of Purkinje cells, estimated to be of the order of 70%, with ballooning of the remaining axons, gliosis of the molecular layer, and demyelination of the white matter. However, n-hexane, responsible for the peripheral neuropathy, may have also contributed to the cerebellar lesions.

Transient cerebellar signs are thus a common feature of acute toluene intoxication, and in some cases more persistent cerebellar abnormalities can occur. The frequency, natural history, and neuropathological substratum of the cerebellar syndrome are unclear, but there is enough evidence to support the conclusion that toluene alone can cause it in cases of severe, prolonged abuse.

(b) *Peripheral neuropathy*

Damage to cranial and/or peripheral nerves has been well documented in subjects who have abused carbon disulphide, MBK, and n-hexane, but the role of toluene in the production of neuropathy is far from clear. Optic neuropathy has been reported in a handful of toluene abusers; in the case described by Channer & Stanley (1983), it was an isolated finding without clinical manifestations, while in others (Keane, 1978; Fornazzari *et al,* 1983), it was associated with cerebral and cerebellar abnormalities in the CT scan, or with sensori-neural hearing loss (Malm & Lying Tunell, 1980; Ehyai & Freemon, 1983). In these cases, the outcome of which has not been reported, toluene was the only substance abused, and it seems likely that it was responsible for the abnormalities.

Peripheral neuropathy has seldom been reported in pure toluene abusers, and the two cases described by Fornazzari *et al* (1983) are the only convincing ones; these patients were considerably older, with longer histories than most abusers, and the symptoms were very mild. The two cases in the series of Streicher *et al* (1981) were also toluene abusers, but alcohol and other drugs may have played an important role.

Added support for the comparatively low risk of peripheral nerve damage in toluene abusers comes from the studies of Shirabe *et al* (1974), Korobkin *et al* (1975), and Towfighi *et al* (1976). These authors all reported the development of peripheral neuropathy in long-standing toluene abusers only when the latter started abusing products containing n-hexane, or when this chemical was unexpectedly introduced by the manufacturers into their preferred brands of adhesive. In one case (Korobkin *et al,* 1975), improvement took place while the subject continued to inhale an adhesive containing only toluene.

The clinical picture of the peripheral neuropathy caused by n-hexane and other VS is fairly constant. Symptoms usually start within weeks or months of exposure, and fairly rapid deterioration continues for some weeks after its cessation. The resulting neuropathy is usually symmetrical and predominantly motor: electrophysiological studies have demonstrated slow conduction velocities and delayed latencies. Paranodal swellings with accumulation of neurofilaments and secondary demyelination have been observed in biopsies of peripheral nerves.

In view of these reports, it seems clear that although toluene may cause optic neuropathy and sensori-neural deafness in a few isolated cases, its potential for causing peripheral neuropathy is low, and considerably less than that of other VS, such as n-hexane, which are no longer present in the adhesives commonly abused. Whether sub-clinical peripheral or cranial nerve damage is present in other toluene abusers remains to be explored.

(c) *Radiological abnormalities*

Radiological abnormalities have been found in some cases of VS abuse by pneumoencephalography (Knox & Nelson, 1966; Sasa *et al*, 1978) or computerised tomography (Boor & Hurtig, 1977; Escobar & Aruffo, 1980; Lewis *et al*, 1981; Ehyai & Freemon, 1983), although normal CT scans have also been reported in equally severe abusers (Kelly, 1975; Malm & Lying Tunell, 1980; Channer & Stanley, 1983). The contribution of toluene to the causation of these abnormalities is difficult to establish, as some of these patients had also abused alcohol and other drugs.

The main radiological abnormalities described are widening of the cerebellar and cerebral sulci and basal cisterns, with enlargement of the ventricular system. These appearances are similar to those described in chronic alcoholics (Ron, 1983), although cerebellar abnormalities may be more frequent in VS abusers. More unusual lesions, such as multiple areas of low density in the cerebral hemispheres reported in one patient who suffered prolonged status epilepticus (Channer & Stanley, 1983), are likely to be due to anoxic or vascular damage, rather than to the direct effects of VS.

The most convincing claim that toluene can produce structural brain changes comes from the study of Fornazzari *et al* (1983): 14 toluene abusers were scanned during the second week of abstinence, and their scans compared with those of 20 neurological patients, reported as normal and matched for age and sex. Using linear measurements, toluene abusers were found to have significantly wider cerebellar and cerebral sulci and larger ventricular systems. The cerebellar abnormalities correlated significantly with the presence of neurological symptoms such as ataxia and tremor, but no significant correlations were found between the severity of the radiological abnormalities and the frequency and duration of toluene abuse. The choice of controls in this study is open to criticism, as the selected scans are unlikely to represent a truly 'normal' population, and could have maximised the differences between the two groups. Despite this criticism, it would be unjustified to dismiss these findings, and it seems likely that in a proportion of chronic, severe toluene abusers, radiological abnormalities may reflect the presence of structural changes in the brain. The neuropathological changes that may account for the CT scan abnormalities are unknown, and the possibility that radiological appearances could improve with abstinence, as is the case in alcoholics (Ron, 1983), needs to be explored.

(d) *Neuropsychological deficits*

The possibility that prolonged VS abuse could cause permanent neuropsychological deficits in a sizeable proportion of subjects is of clear practical importance, but despite scientific and public interest, this question has not yet been satisfactorily answered. The reasons are manifold: to distinguish between acute and chronic effects of abuse, it is necessary to allow for a period of abstinence before testing—something most studies have failed to do; moreover, details of the severity and frequency of abuse are often omitted, making comparisons between studies difficult. Such comparisons are further precluded by the use of many different types of psychological tests, which is a reflection of our ignorance of the deficits most likely to occur. However, the commonest and more serious methodological error is the choice of inadequate control groups. This is particularly important in the case of VS abusing delinquents who, like non-drug using delinquents, are likely to suffer from various learning deficits and specific reading retardation (Wolff *et al*, 1982; Rutter & Giller, 1983). Most of these difficulties could be solved by doing longitudinal studies of populations at risk, and by following-up those who have come to the attention of different agencies, but so far such studies have not been performed.

IQs within the normal range have been reported in uncontrolled (Massengale *et al*, 1963) and retrospective (Skuse & Burrell, 1982) studies of toluene abusers. However using the Halstead

Reitan battery (Halstead, 1947)—a collection of tests reported to be sensitive to the presence of brain damage—Fornazzari *et al* (1983) described cognitive impairment in 16 out of 24 toluene abusers, two days after admission to hospital. In this uncontrolled study, cognitive impairment was found to correlate significantly with the presence of neurological signs and CT scan abnormalities, particularly those in the cerebellum, but these correlations need to be interpreted with caution, as a two-week period had elapsed between the administration of the psychological tests and CT scanning. On the other hand, no significant correlations were detected between the duration of toluene abuse and the severity of cognitive deficits; also, the subjects in this study were older than most reported abusers, and these findings are bound to be different from those of other studies.

Equally contradictory are the findings of some of the controlled studies. An early American report (Barker & Adams, 1963) compared 28 delinquent boys who had abused toluene-containing adhesives with a control group from the same school, matched for age and IQ. The only significant differences between the groups were in the poorer reading ability and school performance of the abusers. Reading ability is often considered to be an indicator of premorbid IQ, and the group differences may have pre-dated the onset of VS abuse; furthermore, the worse school performance of the abusers may have been due to poorer attendance, rather than to cognitive impairment. Similarly, Dodds & Santostefano (1964) failed to find evidence of impairment in a group of 12 toluene abusers tested at least 14 hours after detention, when compared with adolescents from different ethnic and social backgrounds. The authors tried to circumvent the poor matching of the groups by using tests of attention, perceptual vigilance, and visuo-motor skills, considered to be unrelated to age or IQ. Whether these tests were also insensitive to the possible effects of VS is unclear.

More recent studies have reported significant impairment, although methodological errors make interpretation difficult. Berry *et al* (1977) studied 37 subjects (mean age 18) who had inhaled toluene-containing paints for 1.5 to 17 years (mean 5.5 years): those who had brain damage of other abnormalities or who had abused other drugs were excluded from the study; and 11 controls, matched for age and sex and who did not abuse VS or other drugs, were used for comparison. The toluene abusers performed significantly worse in tests of memory and in the Halstead Reitan battery, but the significant difference in IQ between the abusers and non-abusers casts serious doubt on the interpretation of these results. The same criticisms apply to the work of Tsushima & Scott Towne (1977) and of Korman *et al* (1981), who found differences in memory, motor and visuo-spatial skills, and conceptual abilities between poorly matched groups.

Two recent studies in the UK avoided some of these methodological pitfalls, although they are too small to allow definite conclusions to be drawn. Zur (1983) compared 12 delinquent males (mean age 16.4) who had abused toluene-containing adhesives with 12 controls (mean age 14.9), matched for years of education and severity of delinquency. The subjects had been referred either to a child guidance clinic or to the casualty department of a general hospital, and brain damage or other abnormalities had been clinically excluded; both groups had used alcohol and other drugs sporadically. Four subjects, considered to be moderate abusers, had inhaled toluene at least four times a week for a year; the remaining eight, considered to be severe abusers, had inhaled it five or more times a week for more than a year. Testing was performed 12 to 24 hours after the last inhalation and an automated battery that included tests of spatial orientation, psychomotor speed, visual perception, and verbal and visual recognition was used. The groups were well matched for verbal and non-verbal IQ, and when the effects of age were taken into account, the only significant differences were the lesser accuracy of the toluene abusers in psychomotor tests (Digit Symbol Coding), despite their greater speed of response, and their inability to improve test performance in successive trials. Zur (1983) suggested that, given the well preserved memory functions, defective visual scanning may have accounted for these deficits. Neither the severity nor the duration of abuse were related to test performance, and the presence of depression and degree of motivation were not considered to contribute significantly to the differences between the groups.

The conclusions of this study would have been strengthened if independent tests of visual scanning had been used. However, the main difficulty in interpreting the results is in deciding whether the abnormalities detected are the effects of acute intoxication, or whether they represent more permanent neurological deficits. Persistent symptoms such as irritability, insomnia, and fatigue have been reported to last several days in volunteers briefly exposed to 800 ppm of toluene (Von Oettingen *et al*, 1942). Toluene abusers are exposed to higher concentrations for longer periods, and minor deficits encountered less than 24 hours after exposure could be explained on these grounds.

The second study was by Raczka (1983), who selected both toluene abusers and controls from a community home for offenders: the study group consisted of 14 boys (mean age 15.9) who had all abused the same brand of toluene-containing adhesive. The mean reported daily consumption was 300 ml and the duration of abuse 12 to 60 months (mean 30 months). The 15 controls were matched with the abusers for age, social background, severity of delinquency, and reading ability as measured by the New Adult Reading Test (NART) (Nelson & O'Connell, 1978); the subjects were unaware of the specific purpose of the study and the psychologist was blind as to group membership. Tests of IQ (WAIS), motor skill, memory, and language abilities were administered after a self-reported period of abstinence of at least three days (but no blood or urine tests were done to confirm abstinence). No significant differences between the abusers and the controls were found in any of the psychological tests. Moreover, no evidence of intellectual deterioration was found in the abusers group when the scores of the NART (an estimate of premorbid intelligence) were compared with those of the WAIS. The total life consumption of adhesive was not significantly related to test performance.

The flaws in the available studies thus make it difficult to judge whether consistent neuropsychological deficits are present in VS abusers and whether they are transient or permanent in those in whom impairment is suspected. The better controlled studies suggest that if impairment is present, it is mild and limited, although more extensive tests might have uncovered other deficits. It is also possible that cognitive impairment could be detected more frequently if older, more severe abusers such as those recorded by Fornazzari *et al* (1983) were systematically examined. As for the type of psychological deficits most likely to appear in these subjects, our knowledge is equally limited: poor reading ability is almost certain to predate VS abuse rather than follow it, and the use of test batteries that yield a global index of impairment has done little to illustrate the presence of specific abnormalities.

(e) *Psychiatric disability*

Little is known about the prevalence of psychiatric symptoms in this population, and few studies have considered the problem. Behavioural changes and perceptual abnormalities which are common during acute intoxication need to be distinguished from the more enduring sequelae, and pre-existing abnormalities that may lead to VS abuse have to be separated from those that might follow it. Studies in the UK have found different rates of psychiatric morbidity in toluene abusers, depending on the populations sampled: at a special clinic in Glasgow, Sourindhrin & Baird (1984) found that only eight out of a total of 134 cases were in need of psychiatric care, and one-third of these were already receiving it prior to referral. The frequency of psychiatric disturbances was much higher in the study of Skuse & Burrell (1982), who examined retrospectively the records of adolescents referred to the Maudsley Hospital over a three-year period: 45 subjects who had abused toluene-containing adhesives were classified into three groups, according to the duration and severity of abuse. The 16 chronic abusers had consumed on average 250 ml of glue per day for at least six months, while the 14 sporadic abusers had consumed on average 125 ml of glue several times per week in the preceding three months; the remaining 15 had abused adhesives very sporadically, and acted as controls for the other two groups. Approximately two-thirds of the subjects in each group received the diagnosis of conduct or emotional disorder, but there were no significant differences between the three groups in type or frequency of psychiatric diagnosis. The authors concluded that toluene abuse does not appear to be a cause of psychiatric disturbance, but that it occurs in a group of individuals with high psychiatric morbidity.

Similar results have been reported by Lockhart & Lennox (1983); they compared 23 delinquent boys who had abused toluene at least once a week for three months with non-abusers from the same area, matched for age and IQ. Using a questionnaire dealing with psychiatric and psychosomatic symptoms, both groups scored above the cut-off point for the general population, but no significant differences were detected between abusers and non-abusers. These results are in agreement with those reported by Masterton & Sclare (1978) and by Biggs *et al* (1983), but Zur (1983) found depression to be significantly commoner in toluene abusers than in young delinquents used as controls. Although this study was carefully performed, the groups were poorly matched for age, and the results can be explained, at least in part, on the grounds that clinically significant depression is likely to be less common in younger adolescents. Moreover, the reported insomnia and anorexia may have been symptons of withdrawal rather than depressive manifestations.

Although some of the VS abusers reported in the literature were said to suffer from schizophrenia, there is no reason to believe that this condition resulted from the abuse. The cases described by

Alapin (1973) were chronic psychiatric hospital inmates, in whom VS abuse had occurred long after admission, and the same can be said of the patient reported by Lewis *et al* (1981), in whom VS abuse may have aggravated a pre-existing psychosis, but appears unlikely to have caused it.

In populations of drug and alcohol abusers, those who also abuse VS appear to have more severely disturbed personalities, but there is little evidence to suggest that specific psychiatric disability results from VS abuse. Crites & Schuckit (1979) studied a large sample of subjects detained for alcohol-related offences, and classified them according to their use of VS and other drugs: 120 subjects had used VS and other drugs, 411 were polydrug users, but had not used VS, while the remaining 225 had only used alcohol and cannabis. The three groups came from the same geographical area and were of similar age, sex, race, and family background. The VS abusers had more severe drug and alcohol problems than the rest, and received the diagnosis of 'antisocial personality disorder' more often than the other groups, but the prevalence of affective symptoms was the same in all groups, and no cases of schizophrenia were diagnosed. The antisocial activities of the VS abusers preceded the onset of the practice and were considered to be the cause of the more severe drug and alcohol problems. In a comparable study, D'Amanda *et al* (1977) found that heroin addicts who abused VS were more severely addicted to heroin than those who did not abuse VS; suicidal ideation was commoner in VS abusers, but there was no evidence of increased frequency of depressive or other psychiatric symptoms in this group.

The reported rates of psychiatric morbidity therefore vary according to the population under study: they are highest in those referred to psychiatric hospitals and lowest in clients of clinics dealing exclusively with VS abuse. The psychiatric diagnoses in these patients do not appear to differ in type or frequency from those given to well-matched populations of non-abusers, and there is little evidence to suggest that specific or persistent psychiatric disability results directly from this practice. On the other hand, there is little doubt that personality disorders of an antisocial type are common in VS abusers, and particularly in those who also abuse other drugs and alcohol. In these cases, VS abuse is likely to be one more expression of a disorganised, chaotic life-style. The high frequency of psychiatric morbidity in VS abusers appears to be subject to the same genetic and environmental explanations that apply to non-abusers of similar social and family backgrounds.

Some relevant facts from industrial and animal studies

Information gathered from studies of industrial exposure to VS is not immediately applicable to the problems presented by abusers, for a number of reasons. In the first place, industrial exposure occurs for long periods at a time, over many years, and at concentrations lower than those achieved by abusers. Secondly, industrial workers are usually exposed to many more chemicals than is the case in abusers, and the interaction between these substances is likely to alter and/or potentiate their effects. Finally, the age at which exposure occurs in industrial workers differs from that of abusers, and the vulnerability of the two age-groups to the effects of the same VS may be very different. Nevertheless, if permanent cognitive, psychiatric, or neurological disability could be unequivocally demonstrated in industrial workers, similar effects could also be expected to occur in VS abusers.

A detailed review of the studies on industrial exposure to toluene is outside the scope of this paper, but there are some relevant, if contradictory, findings. Hänninen *et al* (1976) compared 33 Finnish car painters to a group of railway workers, matched for age and IQ (as ascertained by tests administered during their military service prior to onset of exposure): the car painters had a mean age of 27 and had been exposed to toluene for a mean duration of 7.4 years. Psychological testing was performed at least 16 hours after exposure; the car painters were found to be significantly worse than the controls in tests of memory, abstract thinking, and perceptual motor skills. Using discriminant function analysis, only 70% of the subjects could be correctly classified into exposed and non-exposed groups according to their psychological test performance; this could be interpreted as indicating a considerable overlap between the groups or as a lack of specificity in the tests used. Although these group differences cannot be ignored in such a carefully controlled study, the possibility that they represent acute effects of toluene still remains.

Two other studies have failed to demonstrate permanent abnormalities in workers exposed to toluene. Struwe & Wennberg (1983) studied 37 Swedish printers who had been exposed to toluene concentrations of 80 ppm (although at times they reached 1000 ppm) for periods ranging from five to 30 years, and compared them to a non-exposed control group matched for age, and professional and educational status. No significant differences were found between the groups in frequency or severity of psychiatric symptoms or in their performance in a battery of psychological tests. However, a third group of painters, who had been exposed to a mixture of VS, had significantly more subjective complaints and more evidence of intellectual impairment than either printers or controls. Similarly, in the UK Cherry *et al* (1982) failed to find significant impairment in a group of 59 workers exposed to toluene concentrations greater than 500 ppm for five years or more, when compared with non-exposed age-matched controls. A trend towards worse performance in the toluene-exposed workers was detected in tests of manual dexterity, speed, spatial ability, and memory, but these non-significant differences may be accounted for by the greater estimated premorbid intelligence (NART) in the control group.

So far, the few studies dealing with isolated toluene exposure in industry have added little to support the possibility that persistent cognitive or psychiatric changes could take place in toluene abusers. The situation may be rather different in workers exposed to mixtures of VS, who are reported to suffer from a variety of 'neurasthenic' symptoms, as well as some degree of cognitive impairment, and to have CT scan abnormalities (Arlien-Søborg *et al,* 1979; Elofsson *et al,* 1980; Juntunen *et al,* 1980; Lindstrom & Wickstrom, 1983). The methodological flaws of these studies, closely linked to the fact that in Scandinavian countries the diagnosis of a psychosyndrome due to exposure to VS leads to financial compensation, make it impossible to draw clear conclusions as to the frequency and causation of these abnormalities.

Equally inconclusive are animal studies, which so far have failed to simulate the conditions of exposure achieved by toluene abusers. Ikeda & Miyake (1978) reported learning difficulties in rats exposed to 4000 ppm of toluene two hours a day for 60 consecutive days. These learning difficulties, also described by Pryor *et al* (1982), who failed to find neuropathological abnormalities in the rats' brains, could be due to sensori-neural deafness rather than to cognitive impairment. Baker & Tichy (1953) described neuronal shrinkage and pigmentation in the cortex, together with fragmentation of myelin, widespread petechial haemorrhages, and loss of Purkinje cells in a dog given intravenous injections of toluene. Whether neuropathological lesions can be consistently produced in the brains of animals who are chronically exposed to toluene remains to be ascertained.

Discussion

The aim of this review has been to examine the possibility that VS abuse may cause neurological, neuropsychological, and psychiatric long-term effects. Special attention has been paid to the effects of toluene, as it is by far the commonest VS abused, so that the possible consequences of this practice could affect large numbers of subjects. Occasional experimentation with toluene-containing adhesives is fairly common in adolescents aged 13 to 16, but is rare after that age. Available evidence suggests that only a minority of those who come into contact with the chemical go on to abuse it regularly, and of these only a few cases come to medical attention with subacute or possibly chronic abnormalities.

To distinguish abnormalities due to acute intoxication from those which represent more permanent damage, a suitable period of abstinence has to be observed before testing patients. The brunt of the acute effects appears to be short-lived, but experimental human studies have indicated that minor non-specific symptoms such as fatigue and irritability may persist for days after a single exposure. Moreover, the elimination of toluene which is bound to brain lipids may take several days; some subacute abnormalities may be attributable to its presence in the brain, even if no traces can be detected in blood or urine. These observations suggest that the few hours of abstinence allowed in many of the studies are insufficient to separate the acute from the chronic effects of VS.

Among the persistent neurological deficits attributed to toluene, cerebellar signs are perhaps the commonest and the most convincingly described. There can be little doubt that a cerebellar syndrome lasting weeks or months occurs in toluene abusers, and that in some cases CT scan abnormalities in the cerebellum can also be detected. However, only a small minority of severe abusers are thus affected, and in milder cases cerebellar signs are clearly transient; in those with more persistent symptoms, improvement has been described with abstinence, although the long-term outcome is not yet known.

It is well known that some VS such as n-hexane can cause peripheral neuropathy, but these substances are no longer present in the commonly used adhesives. Toluene, on the other hand, appears to have a low peripheral nerve toxicity, and only two mild cases in comparatively older abusers can be attributed to it with any degree of confidence. Isolated cases of optic neuropathy and sensori-neural deafness may have been caused by toluene, but whether these abnormalities could be present in a sizeable proportion of abusers, albeit subclinically, remains to be determined.

The enlarged ventricular systems and widened sulci described in the CT scans of some severe abusers may be an indication that widespread structural changes can take place after years of toluene abuse. As with chronic alcoholics, isolated CT scan appearances have to be interpreted with caution, and it remains to be seen whether prolonged abstinence improves the brain shrinkage detected radiologically or whether the abnormalities are permanent. Moreover, the CT scan changes have been reported in an unusually severe, comparatively older group of abusers; whether they can be detected in younger subjects with shorter histories has yet to be determined.

The presence of persistent neuropsychological deficits is even more difficult to evaluate, due to the selection of inappropriate control groups, in addition to the methodological difficulties. It seems likely nevertheless that some degree of impairment was present in the patients reported by Fornazzari *et al* (1983); these subjects also had widespread radiological abnormalities, and seemed to represent the more severe end of the spectrum of abuse. Industrial studies have yielded conflicting results, but the abnormalities in memory, abstract thinking, and perceptual motor skills detected in carefully controlled studies add some support to the possibility that persistent cognitive changes may occur after very prolonged exposure to toluene. Whether these deficits also occur in abusers below the age of 16 is far less certain: the better controlled studies have failed to detect significant impairment, although the numbers involved were too small to allow definite conclusions to be drawn.

Psychiatric morbidity is high among VS abusers, but there is little evidence to consider it a direct result of the practice: the presence of antisocial personality or conduct disorder is likely to be the cause of VS abuse rather than a result of it.

It thus remains doubtful whether VS, and in particular toluene, can cause persistent neurological, radiological, or intellectual impairment in a sizeable proportion of subjects in the age-group commonly involved in the practice. There is, however, some evidence to suggest that these abnormalities can be detected in some severe, chronic abusers over the age of 20. The size of the at risk population in the UK is not known, but so far the practice appears to be limited to a younger age-group. It is possible that with changing patterns of drug use, the number of older abusers will increase, and that the problem of VS abuse could be further complicated by the use of alcohol and other drugs which could potentiate their effects.

Further research in this area is certainly needed. To increase our understanding of the long-term sequelae of solvent abuse, it would be necessary to study a large group of heavy solvent abusers who are at risk of developing persistent neuropsychiatric sequelae. A suitable sample may need to be drawn from different referral sources, such as casualty departments, general and neurological wards, child guidance clinics, drug units, etc. Special attention would need to be paid to the type and pattern of substance abuse, and background social data would need to be carefully collected. To find a suitable control group for such a sample would not be an easy task, but special care should be exercised in matching the subjects for social and educational background and for premorbid intellectual ability by using psychological tests such as the NART (Nelson & O'Connell, 1978). To separate the acute from the more persistent effects of solvent abuse, the subjects should be tested after a period of abstinence of several days—something previous studies have generally overlooked. Toxicological examination of breath or urine samples may be helpful in determining abstinence. Careful psychiatric and neurological examination should be coupled with the use of a comprehensive battery of psychometric tests to detect specific neuropsychological deficits that, if encountered, could subsequently become the focus of more detailed enquiries. Radiological investigations using computerised tomography or some of the newer imaging techniques (Positron Emission Tomography or Magnetic Resonance Imaging) should be mandatory.

The investigation of such a sample should be seen as the basis for a follow-up study that will allow us to determine the progression or otherwise reversibility of the abnormalities encountered, as well as their relationship with continuing abuse or prolonged abstinence.

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Maria A. Ron, MPhil, PhD, MRCPsych, *Consultant Psychiatrist, The National Hospitals for Nervous Diseases, Queen Square, London WC1N 3BG.*

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Political Hazards in the Diagnosis of 'Sluggish Schizophrenia'

HAROLD MERSKEY and BRONISLAVA SHAFRAN

The concept of 'sluggish schizophrenia' is virtually limited to the USSR and some other East European countries, and may contribute to the mis-diagnosis of democrats as psychiatric patients. Recently, a number of articles have appeared in the Soviet literature relating the diagnosis of 'sluggish schizophrenia' or 'slowly progressive schizophrenia' to affective disorders, especially hypomania. Soviet publications on this theme from 1980 to 1984 are discussed, together with their relationship to questions on the abuse of psychiatry.

There have been several aspects to the discussion of the abuse of psychiatry for political purposes in the USSR. In the developed countries it is generally accepted that such abuse has taken place. This was shown in 1983 by the demand from psychiatric societies in such countries as Britain, Denmark, France and the USA for the suspension or expulsion of the *All Union Society of Neuropathologists and Psychiatrists of the USSR* from the World Psychiatric Association. Some people have argued that even if abuse takes place it is important to maintain all methods of professional contact, but that view has now given way to another which holds that formal recognition of societies whose leaders perpetrate abuses reinforces the bad practice; and in any case there can be no benefit to science or to the ethical practice of psychiatry from association with practitioners who disturb or transgress the fundamental rules of the profession.

However, a third consideration has been advanced (Reich, 1981); that the diagnosis which is being misused may be made genuinely, even if we think it is mistaken. This could happen because a society holds a particular view of what constitutes mental abnormality in people who criticise it or break its rules (Lader, 1977). Thus a false diagnosis might arise from a divergence of opinion on what constitutes a psychiatric illness. In other words, the concept of schizophrenia current in the USSR and elsewhere may be the real source of conflict, albeit because of "non-medical needs, preserves and compromises that affect the diagnostic process, but that enter the psychiatrist's awareness to only a partial degree" (Reich, 1981).

In the light of this possibility, we review here a selection of recent Russian publications on 'slowly progressive schizophrenia', with particular reference to articles on its association with affective illness.

The available Russian literature

A number of publications are available in English on Soviet psychiatry (e.g. Snezhnevsky, 1971; Snezhnevsky & Vartanyan, 1970; Holland & Shakhmatova-Pavlova, 1977). More recent attitudes and findings are expressed in the *Korsakoff Journal of Neuropathology and Psychiatry*, which appears to be the principal Soviet psychiatric journal. In two sample years, 1978 and 1983, we have counted 37 and 27 articles respectively on schizophrenia in the *Korsakoff Journal*, representing about one-third of the total number of psychiatric articles. Other psychiatric topics include alcoholism, which gets much attention; epilepsy (usually in the neurological section); oligophrenia; rehabilitation of both neurotic and psychotic patients; manic-depressive diseases; and studies of drugs such as lithium and neuroleptics. Lymphocytes and platelets in various psychiatric states receive a lot of attention.

Amongst the articles on schizophrenia the topic of 'slowly progressive schizophrenia' is popular, and from 1980 to mid-1984 there are 19 publications in the *Korsakoff Journal* primarily or substantially devoted to this theme. All of them come from the USSR except for one from Czechoslovakia. We have found one further article by Soviet authors in *Aggressologie.* At least 13 of these articles are from Moscow. The articles in question are those by Avedisova (1982); Boiarshinova (1982); Boleloutskii (1982); Dubnitskaia (1980); Dubnitskaia & Korsun (1984); Kolesina (1981); Makhova (1982); Mikhlin & Burbulia (1980); Morkovkina (1983); Moroz (1983); Moroz & Nefedev (1982); Rostovskii (1982); Sarsembaev (1983); Sheinin (1983); Shternberg *et al.* (1980); Smulevitch (1980); Smulevitch (1981); Smulevitch *et al* (1983); Sudakov *et al* (1980); and Vilenskii & Kolomiichenko (1983).

All but three of the articles (Boiarshinova, 1982; Makhova, 1982; Smulevitch, 1980) are based upon clinical or epidemiological data. Occasionally, comparison groups are included: for example, Sudakov *et al* (1980) compare the EEGs of 12 patients with sluggish schizophrenia, 11 alcoholics, and also controls. Among the themes discussed in the articles on slowly progressive schizophrenia we find the following: differentiation from other forms of schizophrenia (Sarsembaev, 1983); separation from or relation to manic illness (Moroz, 1983; Moroz & Nefedev, 1982; Smulevitch *et al* 1983); relationship to a hypochondriacal syndrome (Vilenskii & Kilomiichenko, 1983; Avedisova, 1982); relationship with erotomania (Dubnitskaia & Korsun, 1984); relationship with depression (Kolesina, 1981); separation from hysteria (Rostovskii, 1982; Dubnitskaia & Korsun, 1984; Makhova, 1982); and patterns of evolution (Smulevitch *et al*, 1983; Mikhlin & Burbulia, 1980). There is a recurring assumption of an inexorable endogenous process (e.g. Sheinin, 1983; Smulevitch *et al*, 1983).

Special forms are described by some authors. Thus Vilenskii & Kolomiichenko (1983) want to separate hypochondriacal schizophrenia as a disease entity. On the other hand Rostovskii (1982) argues that there are two hysterical variants which should no longer be regarded as involutional hysteria, as originally described by authors like Bumke, Heier and others; instead they should be regarded as manifestations of slowly progressive schizophrenia. This concern with neurotic-like pictures occurs quite often, following the American model of pseudoneurotic schizophrenia now largely abandoned in the West.

Family patterns, prognosis, and treatment by drugs and rehabilitation also receive attention. One worrying difference arises with the discussion of a supposed syndrome of insidiously developing schizophrenia with chronic hypomania, which we consider below at more length. Before that, however, we quote some of the other authors.

Boiarshinova (1982) describes a pattern which we could accept as comparable with simple schizophrenia. She writes of "... the gradual onset and extremely slow course ... absence of overt psychopathological symptoms ... Productive symptomatology ... manifested only by vague asthenic–depressive or asthenic–hypochondriacal syndromes ...' Like others, she emphasises coenaesthopathies, which are not well described. She also emphasises impaired motivation, lowering of empathy, and inadequate social adaptation, with the relative sparing of other learning functions like memory, attention and thinking operations. An additional point is made by Morkovkina (1983), who emphasises a type of slowly progressive schizophrenia with paranoid delusions which appear for understandable psychological reasons and then decline. These patients have very varied premorbid features: some are jolly and industrious, others sensitive, others secretive and suspicious. In the early phases of the illness, reticence, self-consciousness, withdrawal and a dreamy attitude are noted, combined with demands for increased attention and emotional coldness towards the family. Blunted affect is said to appear later. Again we can recognise formulations which could apply to our own diagnostic schemes, but with occasional differences.

However, things get complex and diverse. Morkovkina comments that from 20 to 25 years of age blunted affect is complicated by the appearance of disturbances such as hypochondriacal fears or unstable ideas of reference. From then on, a tendency towards over-valued ideas "could be noticed in the patients and with time they gradually became people of over-valued ideas dedicated to fixed rules which virtually did not change during the rest of their lives". This tendency to over-valued ideas is seen to be a manifestation of the schizophrenic process in most of the patients. Some patients, dreaming about "great love" and fantasising about it, concentrate all their attention on their partner, after starting family life with excessively solicitous behaviour and demands for the same from the spouse. Others become workaholics in their mature years: they demonstrate "boiling-over" energetic activity in their field of work or dedicate themselves to "over-valued hobbies". The usual responsibilities of the family and the household do not interest this group. Morkovkina also notes all types of delusional reactions, including prolonged paranoid reactions, sub-acute paranoid reactions, and acute reactive paranoias, in her group with slowly progressive schizophrenia, even though these are usually separated from schizophrenia as such. Some patients "kept their scientific discoveries in secret for fear of their competitors stealing and using them". She concludes that psychological causes "did not have a big role in the slow progression of the schizophrenic process".

A more pragmatic approach appears with the Czech author Boleloutskii (1982), who reports on the drug treatment of 208 patients with slowly progressive schizophrenia. Amongst this group there were 125 with 'neurasthenic conditions' and 51 with 'neurotic depressions'. (This suggests to us that progressive schizophrenia is diagnosed unusually frequently compared with simple schizophrenia in the West.) Levomepromazine was given to 15 patients and alleviated 22% of their symptoms. Dothiepin was given to 25 patients and eliminated 9% of symptoms, and diazepam eliminated 5% of symptoms when given to 16 patients. Thus levomepromazine was held to be statistically more effective in eliminating the symptoms. Some patients were also said to show symptoms of the borderline states, and it was found that those with uncomplicated slowly progressing schizophrenia responded to psychotropic drugs differently from those with presumably concurrent borderline states. Accordingly, Boleloutskii thinks that patients with slowly progressing schizophrenia have a specific biological basis for the disease, that determines the type of response to medication. While this approach appears to be a pragmatic one, it is by no means systematic, nor impressive in its examination of data.

A fourth author, Makhova (1982) refers to the problem of early and precise diagnosis of slowly progressive schizophrenia as being very important and complex. She notes that it is particularly important in cases with early manifestations of negative symptomatology (which is particularly pertinent for this disorder) when there are states resembling psychopathic conditions. The question of timely diagnosis of slowly progressive schizophrenia is held to be "directly related to the prophylaxis of socially dangerous actions because most patients come in contact with a psychiatrist only after a law-breaking act has been committed". Extreme emotional instability is described, with a tendency towards frequent spontaneous mood swings and inadequate reactions towards provocative events ("irritants"). Elements of "diffusely paranoid mood", falling short of formal delusional ideas, are noted in some patients during the peaks of their emotional swings. During periods of elated mood, the patients are lively and increasingly active; outside those periods, they are "flaccid, in a sense inadequate, and unable to push the practical matters important to them to the final resolution". They have a short attention span, changing short-lived interests, and an inability to maintain concentration of the will for long periods of time. These phenomena, together with extreme emotional instability, are held to make the patients' behaviour difficult to predict, to interfere with socially useful work and to promote a failure of adaptation by the patients. The disturbances of thinking typical of all types of slowly progressive psychopathic-like schizophrenia are characterised by the author as having the following major manifestations: "Distortion of the process of integration and of logical operations because of the influence of affective swings (literal translation: 'moments'); rigid, disconnected, biased rules and estimates and the impact (literal translation: 'actualization') of important personal matters". "Uneven disturbances of the thinking process" are also observed in conjunction with the relative preservation of some types of thinking (constructive, calculations, some logical operations). In an argument which we could not follow, the author talks of "correlation of the manifestations of the disorders of thinking from the character of tasks, their 'personally neutral' or 'personally important' context". In all these patients there is said to be polymorphism of the thinking disorders.

Illegal acts are committed not during the initial states of the disease but during the period when pronounced and clinically defined psychopathic-like manifestations appear: "Thus, the degree of social maladaptation is one of the most important parameters allowing us to estimate the risk of law breaking".

These examples give some flavour of the writing and the ideas which the authors favour. The notion of slowly progressive schizophrenia is clearly widely extensible and is much more variable and inclusive than our own ideas of simple schizophrenia or residual defect states. Many conditions which would probably be diagnosed elsewhere as depressive disorders, anxiety disorders, hypochondriacal or personality disorders seem liable to come under the umbrella of slowly progressive schizophrenia in Snezhnevsky's system. The importance of this diagnosis applied to questions of legal responsibility scarcely needs emphasis. It enables very many people to achieve immunity from punishment, but only at the price of being diagnosed as insane and perhaps treated accordingly. It is common for Soviet psychiatric descriptions, like those in the West and in other countries, to contain many terms which correspond to what is found, or reported on, in individuals who are considered to be normal. 'Jolly, active individual', 'temporary disturbance of concentration', 'mere emotional instability', 'unemployment', 'personal rigidity', 'some withdrawal' are all terms which may be applied to numerous people who ought not to be considered to be psychologically ill. Accordingly, there is real reason to suppose that the widespread employment of the diagnosis of 'sluggish schizophrenia' with such poorly defined boundaries is liable to lead both to the misdiagnosis of people who have neurotic disorders and to the erroneous labelling of normal individuals as sick. Where sluggish schizophrenia is supposed to be associated with hypomania this risk seems to arise quite strongly; this possibility is considered at more length below.

Relationship to hypomania

Moroz (1983) describes 44 patients suffering from 'slowly progressive schizophrenia with affective disorders'. A long latent stage is defined as Bonn's (sic) 'masked mania' (Bonnet, 1979) and two variants are described which we outline below.

Introductory remarks by Moroz refer to comments on hypomania by Wernicke (1923) and Korsakoff (1901), and to an association between chronic hypomania and schizophrenia noted by Mayer-Gross *et al.* (1960) and by Kondratiev (1977). German references (Specht, 1908; Ewald, 1925) and other Soviet sources demonstrating the combination of schizophrenia and hypomania are cited.

The age- and sex-distribution of Moroz's sample is stated next (range 34–75 years; 19 M, 25 F) and it is indicated that the subject population all had schizophrenia preceded by an affective illness, usually "masked mania" after Bonnet (1979). Moroz writes: "Bonnet used this term for a special type of hypomania, where symptoms were masked by the neurotic disorders and behavioural disturbance. But according to the author of the present study, any psychopathologic factors may serve as 'masking'."

Chronic hypomania is then described: according to Moroz the elated affect of chronic hypomania is characterised by firm optimism, great energy and a boundless belief in one's own abilities. The patients liked dealing with people and organising different activities. They were alert and energetic, slept 5–6 hours a night, easily tolerated an increased workload, and participated in many committees. It is said that they over-estimated their individual and business qualities and were sure of their ideas and actions being correct. All these characteristics resemble 'constitutional hyperthymia'. However, Moroz maintains that his patients lacked the ability to switch quickly and did not show rapid change of interests nor romantic attractions. He adds: "Their activity took place within strictly defined borders; they did not exhibit sudden thoughtless actions; their communicability was often of a formal character."

In addition to chronically elated affect, the patients had over-valued ideas, most often in the professional sphere. These are described as follows: "Inventing and improving different plans, the patients were fully engulfed in work, did not rest on weekends and holidays, and could talk only about their 'hobbies' because other topics seemed boring to them. The patients were firmly convinced that their activity was interesting for everybody and did not allow any irony regarding their work. In some cases the content of over-valued ideas was outside their main occupation". Examples are given of artefacts made from unusual materials, a special method of wood carving designed by the patients, and poetry. It is said that "some patients organised groups, trying to involve as many participants as possible, and tried to spread their ideas. Others, believing that they should be involved in educational activities, were organising clubs and libraries. No obstacle could stop them. They managed to get financing, room and equipment for their projects". Moroz claims that the descriptions of over-valued ideas by Wernicke (1923) and Bumke (1924) stress that the content does not change in decades. In his own cases, however, over-valued ideas altered: prominent ideas, formed in the phase of chronic hypomania, changed several times during the decades of the disease.

Moroz describes a variety of neurotic phenomena linked with chronic hypomania; and besides neurotic symptoms, overt mania was diagnosed in seven patients, depression in twenty, and bipolar illness in three. A slow pace of progression of negative changes is emphasised, and differences from pseudoneurotic schizophrenia are mentioned. Moroz adds: "most patients (37 people) had increasing rigidity, pedantry, circumstantiality, and inability to orient themselves quickly in rapidly changing situations. These qualities were associated with thoroughness at work. The patients were very thorough and kept special files, albums, or card indexes and became irritated if somebody ruined their 'system' ... In seven cases psychopathic-like changes with predominant explosive features—roughness, aggressiveness of behaviour, lack of manners and of the sense of distance (i.e. conspicuous lack of respect towards those above in the hierarchical system)—were obvious."

Moroz suggests that latent schizophrenia "corresponds to the clinical period characterised by chronic hypomania". He says that Bleuler (1911) wrote about the possible "hidden" latent course of the schizophrenic process, during which all symptoms characteristic of the clinical form of the disease are present in rudimentary form. But the overall clinical picture Moroz describes is a mixture of different neurosis-like, psychopathic-like and affective disorders, in some cases constantly present and in others appearing in exacerbations. In his cases, phases are recognised against a background of markedly elated affect and a wide variety of pseudoneurotic manifestations (obsessiveness, phobia, "coenesthopathia", etc.).

The latent period, in Moroz's sample, lasted 12–49 years (mean 27 years), and was usually more than 20 years. The change into the active period of the schizophrenic process occurred at the age of 23–69 years but usually after the age of 40.

Two variants of slowly progressive schizophrenia are described next; the first with depression, the second with delusional disturbances. In the first variant the patients complained of apathy, flaccidity, being tired easily, lack of desire to do anything, lack of confidence in their own abilities, and difficulties in communicating with people; but, curiously, their self-esteem remained high, they behaved with a sense of superiority, and they praised their achievements and the good features of their own character.

In the second variant, delusions are described: "Ideas of reforms and inventions, sometimes associated with legal complaints, and delusions of persecution of small degree were predominant in our cases". Two cases had love-related delusions and two cases had both delusions of jealousy and hypochondria. "Delusional content had a usual content [sic], there were no ridiculous ideas completely detached from reality."

Moroz sums up by emphasising the similarity of the course of this illness to that of the affective psychoses and he claims that an atypical affective disorder is the main clinical manifestation of slowly progressive schizophrenia. He indicates that the atypical quality is exemplified by the occurrence of pseudo-neurotic and delusional symptomatology and strong features of affective disturbance. The disease is held to have a very long latent period and "only transitory exacerbations testify to the fact that it is present, whilst there is no well-defined periodicity of the psychopathologic manifestations in the active period". Besides the fact that the patients showed obsessional and other neurotic disorders in different sequences and mixtures, "psychopathologic symptomatology was not stable, was polymorphic and changed. Delusions appeared on their own and were also provoked by situations, they were not subject to systematisation and extension".

Moroz finishes with five references to other workers, including Leonhard (1957), who have described atypical or chronic hypomania or commented upon it.

The ideas which Moroz puts forward are shared by some of his colleagues from the same department. Professor A. B. Smulevitch is the head of that department (the third clinical department in the All-Union Institute of Psychiatry, Moscow) and Professor A. V. Snezhnevsky is the head of the Institute. In an article in the same journal, Smulevitch *et al* (1983) write on "psychopathic-like" states in schizophrenia, and comment on features which Moroz describes, like sustained elated affect without distractibility or change of interests. Smulevitch *et al.* also refer to patients who "... enjoy the reputation of careful qualified specialists. At home and at work they are concise, always well balanced, productive and active, so that one may get the impression that emotions do not play a role in their motivational behaviour and that all their actions are dictated by cold calculation ... (they develop) ... 'hypochondria of health' ... lead an ascetic way of life, quit smoking, refuse to drink alcohol, and try to follow the advice of physicians or doctors' recommendations from the popular medical literature".

Like Moroz, these authors describe many phenomena which are not in themselves abnormal; furthermore, 103 of their 111 patients returned to work but were still regarded as being schizophrenic. First-rank symptoms of schizophrenia are not discussed, and diagnostic features such as hallucinations and overt delusions which figure in ICD-9 and DSM-III are barely mentioned in passing.

Discussion

If the articles we are considering had been submitted in English to a Western journal, most of them would probably have been returned for radical revision. As noted above, the original writing is diffuse and cumbersome: we have attempted to make some of it more readable in translation. At times the writing is also disturbingly incomprehensible, even to readers who grew up speaking Russian and received a Russian medical education. Furthermore, the articles are often not arranged in a conventional pattern. The hard factual data provided may consist of only a minimal demographic account of the patients, scattered throughout the text. The account of the disorders themselves is often repetitious and hard to follow. Reliability studies are absent. No criteria for diagnosis are specified: these have to be inferred from lengthy descriptions. The need for replication by other observers is never considered; instead, we have the authors' views and their observations as to where they differ from the findings of others, and it is assumed that this is enough. Their experience is taken to be veridical.

References to the literature in Russian, English, French and German are more impressive. The concepts of Moroz, for example, are interesting and can be substantiated (at least partially) by the literature to which they refer. Some doubts arise, however, as to the accuracy of the author's knowledge. Moroz comments on Mayer-Gross *et al* (1960) to the effect that they have described prolonged hypomanic conditions occurring during the earliest phases of schizophrenic processes. In our reading of Mayer-

Gross *et al* in the section and edition cited, they merely note that in some patients with atypical affective illness, or with affective illness that has some schizophrenic admixtures, a chronic schizophrenic picture emerges with progressive deterioration. Elsewhere in the same work they emphasise that attacks of depression or elation are usually short-lived in schizophrenics and that actual combinations of manic–depressive and schizophrenic disorders can be traced to a combination in the patient of schizophrenic and affective genetic factors coming from different sides of the family. Referring to the schizophrenic patient with only a brief affective episode, they say "to segregate him from other schizophrenics, as having a disorder of an aetiologically distinct kind, can only be a source of confusion, and leave one without the foundation of treatment or prognosis. No observer has been able to show that over a prolonged follow-up study, the outcome of these states differs from that of the generality of schizophrenia". The gist of the writing by Mayer-Gross *et al* is that they would not be willing to accept a diagnosis of schizophrenia in patients who did not have quite good signs and evidence confirming that diagnosis. As they say in their third edition (1969: page 221), a diagnosis of the combination of two psychoses "... should be made only when there is strong positive evidence on both sides". Similarly, Moroz cites Nunn (1979) as holding the view that "complex clinical pictures like this" are a result of a combination of hypomania and atypical depression, but it is not in fact clear to us from examination of the paper by Moroz and that by Nunn that the latter envisaged anything like the pattern which Moroz describes, although Nunn is concerned both with protracted bipolar illnesses and intervening schizophrenic disorders. We thus have the impression that the British literature, and other literature as well, is being cited in a rather tangential fashion, and unjustifiably, to support Moroz's own views.

More importantly, Moroz cites Hamel & Vernet (1921) as saying that the delusions of the second variant "... had several characteristic features—not much of the systematisation and changing story line". Those authors, writing about patients with chronic hypomania combined with a chronic delusional state, actually say "... *le délire n'a rien perdu ni de sa systématisation ni de sa vigeur*": we take this to mean that the delusional state loses neither its systematic features nor its strength in such cases. It seems that Moroz is not quoting the source accurately.

It appears that illnesses which we would believe to be true manic or schizo-affective are being confounded with whatever Moroz regards as "insidiously developing schizophrenia accompanied by the manifestations of chronic hypomania". In fact there is no worthwhile link in phenomenology (nor in our experience) for the unity between normal-seeming conditions and psychoses which Moroz appears to be trying to establish.

The effort to demonstrate that unity, however, could be regarded as an appropriate scientific endeavour if one accepted Snezhnevsky's ideas (e.g., Snezhnevsky, 1971): the Soviet approach to schizophrenia places great reliance on the diagnostic system introduced by Professor A. V. Snezhnevsky, the acknowledged head of Soviet psychiatry and the leader of the institute where Moroz works. Snezhnevsky's system has been described in English by himself (Snezhnevsky, 1971; Snezhnevsky & Vartanyan, 1970) and by a number of American workers, especially Holland & Shakhmatova-Pavlova (1977) and Reich (1981). Reich (1981) provides good documentation of the other sources. Much of Snezhnevsky's system is acceptable in terms of DSM-III, but some types of "sluggish" and "shift-like" schizophrenia present great problems. In the former the patients are neurotic, self-conscious, introspective, and troubled with obsessive doubts, conflicts with parental and other authorities, and "reformism". In "shift-like schizophrenia", which is also known by the German word *"schubweise"*, the patients are neurotic, with affective colouring, social contentiousness, philosophical concerns and self-absorption.

Snezhnevsky lays much emphasis on ideas of evolution in which successive syndromes are seen as manifestations of one disease in which asthenic and affective elements are early features. He considers that there can be no strict boundaries between manic–depressive psychosis and schizophrenia. He states further that the early disturbances may resemble neurotic or personality changes ("psychopathic states" in his terminology) and that the genetic relationships of "psychopathic personalities" with schizophrenia need investigation. (We assume that he is using the term "psychopathic personalities" in the continental European sense of neurosis or personality disorder which is not necessarily sociopathic). Snezhnevsky does not provide good operational criteria for defining his cases and it is alarming to reflect on how the diffuse descriptions of personality changes and schizophrenia found in the accounts of his diagnostic system could be applied out of context to people who actually lack the additional explicit irrational manifestations which are required by DSM-III as proof of psychosis.

Acute schizo-affective disorders are a matter for attention in the West; and the association of depression with schizophrenia is an important theme, particularly the possibility that it might be caused by neuroleptic medication (e.g. Johnson, 1973). But in any case, in Western countries depression is often held to precede or accompany schizophrenia. The differential diagnosis of mania and schizophrenia is also a recognised issue. An association of chronic hypomania with schizophrenia is a more contentious topic, and perhaps we could benefit from some discussion of it: but if that was all that was to be said about this article, it would not justify our attention, because it is significantly below the standards of modern scientific psychiatry even though it has appeared in the leading Soviet journal of psychiatry. Similarly, although the relationship of psychosis with personality disorder is a prominent topic in our literature, the diagnosis of psychosis on the basis of personality disorder alone is rejected in the West.

The importance of the article by Moroz lies in the description of the behaviour which is prominently associated with psychosis. Some of it—for example, love delusions, ideas of worthlessness, marked depressive affect or overt mania, phobias and formal obsessive–compulsive symptoms or ruminations—would be acceptable to us as evidence of psychiatric illness, although not necessarily as evidence of psychotic illness in all cases. The features of Moroz's first (depressive) variant of slowly progressive schizophrenia on the other hand seem rather odd, and command less ready acceptance. However, the more subtle changes reported raise much greater issues. Over-valued ideas are deliberately defined as such because they cannot be said to be delusions. It is for that reason that they are hard to use as evidence of irrationality sufficient to justify, for example, a change of legal status. Other features of the descriptions might characterise some very successful members of any group; "Firm optimism, and boundless belief in one's own abilities ... alert and energetic, slept five to six hours per day, easily tolerated an increased workload and participated in many committees ... they were sure of their actions being correct ... similarity ... with constitutional hyperthymia ... lacking in the ability to switch quickly, diversity, rapid change of interest and romantic attractions ... did not exhibit sudden thoughtless actions". When this description is linked to the idea of a slowly progressive, insidious state that can be hard to recognise, the possibility of political abuse of the psychiatric schema becomes formidably great.

It is true that somewhat similar descriptions may occur in our own textbooks. It is common for English writers to consider that at least 20% of the general population may have psychiatric disorders (Shepherd *et al*, 1966; Goldberg & Huxley, 1980) and the figures quoted are sometimes much higher (Srole *et al*, 1962). But these are self-disclosed symptoms and complaints, not disorders which the 'patient' himself rejects and which his relatives may also reject. Moreover, in both DSM-III, which is admirably specific in its requirements, and in ICD-9, clear criteria are described for major psychoses. Thus the more normal-sounding descriptions of patients should not be used for diagnostic purposes unless convincing evidence of more impressive psychotic phenomena is also available. In the absence of overt psychotic symptoms (e.g. hallucinations, gross thought disorder or classical hypomanic elation plus flight of ideas, etc.) we do not feel comfortable in making a diagnosis of schizophrenia or hypomania solely on the basis of these more subtle and arguable clinical phenomena. The latter can rarely, if ever, be held to justify compulsory committal.

Unfortunately, this is not true for the Soviet practice of psychiatry. Prominent dissidents like Leonid Plyushch (Khodorovich, 1976) and General Grigorenko (Committee on the Judiciary, US Senate, 1972) have been characterised as having "reformist delusions". The discussion of Plyushch under the chairmanship of Dr Snezhnevsky is reported to have contained the following comments: "recent symptoms include the appearance of inventive ideas in the field of psychology ... his stable concern with reformism has been evolving into a concern with innovation in the field of psychology ... He should be sent for compulsory treatment in a psychoneurological hospital". Plyushch was a cyberneticist and his interest in the design of games developed in relation to his wife's interest as a child psychologist. He also wrote a number of fairy tales which he included in letters to his children that never arrived. In Grigorenko's case the 'reformist delusions' were part of a political campaign which he conducted ardently but without any impropriety or violence. When a psychiatric system places such emphasis on *latent* illness, which is used to justify detention but is not detectable by our usual open techniques, it involves immeasurable risks to individual liberty.

Plyushch was seen by three senior Fellows of the Royal College of Psychiatrists who reported on their observations in March 1976 (Royal College of Psychiatrists, 1976). They did not examine him formally, but noted "no indication of schizophrenia or other mental illness in an idealistic young man". In the same month, one of us (H.M.) explored with Mr Plyushch whether he had had any unusual hallucinations or schizophrenic-like experiences, and found no specific evidence of any positive signs of schizophrenia or their previous occurrence. Plyushch gave a dignified and tolerant reply to a question about why he was prepared to face the risks involved in membership of the dissident movement: his comment was that he could not live with himself if he were to hold back from taking part once he had begun to be aware of the issues involved.

Grigorenko was examined at his own request by three leading American psychiatrists, who concluded that he had been rational and mentally healthy throughout (Reich, 1980).

Given Snezhnevsky's diagnostic criteria, and without the discipline of having to prove the presence of overt psychotic phenomena, anyone with any spark of social concern can be defined as 'mad'. It is also questionable how many psychiatrists or psychologists with innovative ideas in the field of psychology can safely be left at liberty.

Soviet psychiatrists are aware of some of the discrepancies between their system and others. Reich emphasises that the International Pilot Study of Schizophrenia (WHO, 1973) demonstrated at Snezhnevsky's own centre that differences from other centres rested upon the frequent diagnosis in Moscow of 'sluggish schizophrenia' when the recommended ('computer') diagnosis was manic illness, depressive psychosis or, most often, depressive neurosis. It is thus a matter for concern that some of the authors cited couch their findings in terms of standard Western diagnostic systems without noting important differences of approach. To be charitable, one might suppose that they intended to reconcile the divergences. However, the Soviet system is often presented in their articles as a way of understanding diagnostic problems which is compatible with the approaches found in the Western literature. There is no hint of a pre-existing conflict, and the Soviet reader might easily by misled in consequence.

Yet even from within the USSR criticism of the Snezhnevsky system has been voiced by at least one author writing in the professional literature (Kazanetz, 1979) and, of course, by others like Gluzman and Koryagin, who have been imprisoned. Kazanetz (1979) has criticised the Snezhnevsky system and said that it leads to an over-diagnosis of schizophrenia because it tends to identify those with exogenous psychoses as chronic schizophrenics. Kazanetz seems since then to have lost his job (Bloch & Reddaway, 1984).

The position of a group of Soviet experts was once stated as follows:

> "There is a small number of mental cases whose disease, as a result of a mental derangement, paranoia and other psychopathological symptoms, can lead them to antisocial actions which fall in the category of those that are prohibited by law, such as disturbance of public order, dissemination of slander, manifestations of aggressive intentions, etc. It is noteworthy that they can do this after preliminary fabrications, with a 'cunningly calculated plan of action', as the founder of Russian forensic psychiatry V.P. Serbsky, who is widely known for his progressive views, wrote: *'To the people around them such mental cases do not create the impression of being obviously "insane".'* Most often these are persons suffering from schizophrenia or a paranoid pathological development of the personality. Such cases are known well both by Soviet and foreign psychiatrists.
>
> The seeming normality of such sick persons when they commit socially dangerous actions is used by anti-Soviet propaganda for slanderous contentions that these persons are not suffering from a mental disorder." (Schmidt *et al*, 1973).

The 21 people who subscribed to this view were members of the presidium of the All-Union Society of Neurologists and Psychiatrists of the USSR.

To return to the articles which we have reviewed, it appears that under the influence of an unscrupulous regime the observations they put forward could serve as a ready means to label as psychotically ill many energetic and capable citizens who were in disagreement with authority. The observance of well defined standards of diagnosis and evaluation, such as are routine in Canada, the United Kingdom and the United States, could prevent abuse. Such possibilities are specifically bypassed by Schmidt *et al* (1973); nor are they evident in the article by Moroz. Indeed, some of the opinions which we have quoted are particularly frightening when one considers that they are being applied to people who are functioning well or perhaps only with some evidence of neurosis: "Some patients organise groups ... room and equipment for their project" (Moroz: *vide supra*). They allow for the psychiatric disposal, without much other justification, of anyone whose social activism is unacceptable to the psychiatrist who believes in the officially-approved system.

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*Harold Merskey, DM, FRCP, FRCP(C), FRCPsych, *Professor of Psychiatry, University of Western Ontario; Director of Education & Research, London Psychiatric Hospital, 850 Highbury Avenue, P.O. Box 2532, Terminal "A", London, Ontario, Canada N6A 4H1.*

Bronislava Shafran, MD, *3450 Wayne Avenue (Nr 15A), Bronx, New York 10467, USA; Resident in Neurology, Albert Einstein College of Medicine, Yeshiva University, New York, USA.*

*Correspondence

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The Endogenous Sub-type of Depression: A Study of its Internal Construct Validity

MICHAEL A. YOUNG, WILLIAM A. SCHEFTNER, GERALD L. KLERMAN, NANCY C. ANDREASEN and ROBERT M. A. HIRSCHFELD

The internal construct validity of the endogenous sub-type of major depression was investigated by statistically modelling the RDC endogenous and DSM-III melancholia diagnostic criteria. Data consisted of symptom ratings on 788 patients with major depression from NIMH Collaborative Depression Study. Results indicated that the symptoms in the criteria do not specify a dichotomous classification, melancholic-non-melancholic or endogenous-nonendogenous. Results did support the existence of two sub-typings, one related to anhedonia, and one related to vegetative symptoms. The vegetative sub-type rarely occurred in non-anhedonic patients. Previous studies may have found support for a simple endogenous sub-type because of this hierarchical relationship and as a result of methodological differences.

The concept of an endogenous sub-type of depression has a long history in psychiatry (Gillespie, 1929; Kendell, 1976). It has had a number of different meanings (Klerman, 1980; Hirschfeld & Katz, 1978), including differentiating those depressions which: are not precipitated by stress; are biological in aetiology; are not responsive to environmental events: are responsive to biological treatments; occur in patients without personality pathology: and exhibit a particular pattern of symptomatology. This last approach has been taken by the Research Diagnostic Criteria (RDC: Spitzer, *et al*, 1978) and the third edition of the Diagnostic and Statistical Manual of the American Psychiatric Association (DSM-III; American Psychiatric Association, 1980). Patients are classified according to a set of symptom criteria; the resulting classification is then expected to correlate with some or all of the other "endogenous" characteristics, providing external validation of the diagnostic criteria. However, attempts to obtain these correlations have met with mixed results.

To develop sub-typings of depression which will be validated by clinically meaningful external validators, we must have diagnostic criteria which are internally consistent both theoretically and logically. This paper examines the internal construct validity of the endogenous concept by evaluating diagnostic criteria. By internal construct validity, we mean that the rules for classifying patients are consistent with the concept of diagnostic criteria, i.e. (a) that the specified clinical features are jointly indicative of an underlying classification, (b) the classification is inferred from the clinical features, and (c) that the relationships between the clinical features and the diagnostic classes are those indicated by the rules of the diagnostic system. If a diagnostic system is valid, it must reflect these criteria. Although the diagnosis itself is not directly observable, such symptom-diagnosis structures can be investigated statistically. Furthermore, since these structures have quantitative implications for the relationships among the observed symptoms it is possible to measure how well these structures explain the empirical data. Correlations of external validators with sub-typings based on internally valid diagnostic criteria are then more likely to be observed and replicated.

This study first examined the internal construct validity of the RDC criteria for the endogenous sub-type and, as relabelled by the DSM-III, critiera for the melancholic sub-type. Alternative classification schemes, suggested by the data were also evaluated. A synthesis of the differences between the symptoms included in the criteria were reconciled in an analysis, synthesising the two sets of results, in order to produce new sub-types and criteria.

Method

Subjects and data collection

The sample subjects consisted of 788 depressed patients from the Collaborative Study on the Psychobiology of

TABLE I

DSM-III Melancholia and RDC endogenous criteria: required SADS *symptom scores and symptom base rates*

Symptom	*DSM–III Melancholia**	*RDC Endogenous***	*SADS Item*	*Criterion*	*n*	*%*
Loss of pleasure	—	B	326	≥3	763	97
Pervasive loss of pleasure****	A	A	326	≥5	564	72
Lack of reactivity	A	A	350	≥5	601	76
Decreased appetite	—	B	317	≥3	555	70
Weight loss	—	B	319	≥3	392	50
Decreased appetite or weight loss	B	—	317 or 319	≥3	580	74
Terminal insomnia	B	—	275	***	452	57
Terminal or middle insomnia	—	B	275 or 274	***	590	75
Psychomotor agitation or retardation	—	B	342 or 334	≥3	531	67
Marked agitation or retardation	B	—	342 or 334	≥5	93	12
Distinct quality of mood	B	A	236	≥3	563	71
Worse in the morning	B	A	351	=4	288	37
Guilt	B	B	240	≥3	601	76

*Criteria require both A symptoms and at least 3 B symptoms.

**Criteria require at least one A symptom and at least 4 symptoms total for "probable," at least 6 symptoms total for "definite."

***Specified type of insomnia present and global insomnia (SADS 272) score of ≥3.

****Loss of pleasure in all or almost all activities. Less than pervasive loss consists of loss of pleasure in at least some activities.

Depression (Katz, *et al*, 1979). At admission to the study, all patients were assessed using the Schedule for Affective Disorders and Schizophrenia (SADS) (Endicott & Spitzer, 1978), including information on the presence or absence of the criterion symptoms for endogenous and melancholic sub-types. The symptom criteria and corresponding SADS items and scores are shown in Table I.

Of the patients 464 (59%) were female; the mean age was 38.7 (s.d. = 14.5) years; 610 patients (77%) were in hospital, 189 (24%) were bipolar, 432 (55%) were primary, and 133 (17%) were psychotic. Endogenous and melancholic patients were relatively heavily represented; 237 (31.4%) were both endogenous (definite) and melancholic, 246 (32.5%) were endogenous but not melancholic, 14 (1.8%) were melancholic but not endogenous, and 259 (34.3%) were neither endogenous nor melancholic.

Since the two sub-type criteria are applicable to specific, but somewhat differently defined, major depressive groups, it is important that we specify the subjects available for our study and which were employed in the analyses. The data collection predates DSM-III and was organised around the RDC. Since an RDC diagnosis of definite major depressive disorder was required to enter the study, subjects with only four of the eight associated symptoms of the depressive syndrome, who would meet DSM-III criteria for major depression but only probable criteria under RDC, were never admitted. DSM-III does not include impairment or duration requirements and counts either self-reproach or negative self-evaluation, whereas the RDC includes only the former, so that there are some patients with DSM-III depression (for the most part the milder ones) who are not included in our sample.

By DSM-III criteria, most RDC schizo-affective-depressed patients would receive a diagnosis of major depression. Therefore, patients with an RDC diagnosis of either major depressive disorder ($n = 756$) or schizo-affective disorder, depressed type, primarily affective ($n = 32$) were included in the melancholia analyses. (Re-analysis with major depressive disorder only led to identical results). The RDC endogenous criteria do not apply to schizo-affectives and so, in the analysis of endogenous criteria, only patients with major depressive disorders were included ($n = 756$). In the analyses synthesising the results, only RDC major depressive disorder was included.

Both the RDC endogenous and DSM-III melancholia subclassifications are applied to *episodes* of major depression, so that they apply to patients with both unipolar and bipolar histories. Eleven patients who exhibited manic and depressive symptomatology simultaneously were excluded, since this condition might unpredictably alter their depressive syndromes. It should also be noted that DSM-III allots one digit for coding subtypes, and therefore records the more 'clinically significant' of melancholia or psychotic features. Since this is an artefact of the coding scheme, rather than a theoretical statement about the relationship between psychotic and melancholic depression, we have included in our analysis psychotic as well as non-psychotic patients.

Statistical analysis

The concept of diagnostic criteria makes the basic assumption that the presence, or absence of each of a set of observed clinical features is indicative of the presence, absence of an unobserved diagnosis. Latent class analysis (LCA) provides a mathematical model of these structural relationships (Young, 1983; Young & Tanner, 1983). The adequacy of this model can then be tested using empirical symptom data. LCA allows us to quantify various aspects of the proposed diagnostic classification, despite the fact that it cannot be directly observed. LCA is conceptually similar to the 'point of rarity' approach (Kendell, 1975, Kendell & Brockington, 1980) for cases in which symptoms are considered to be present or absent and considered multivariately, i.e. not reduced to a single score.

LCA models represent the structure of diagnostic criteria by specifying that a set of symptoms is inter-related by virtue of each symptom being related to the same unobserved diagnostic classification; e.g. endogenous symptoms occur in a particular pattern because each symptom is related to the endogenous sub-type. If the observed symptoms were unrelated, i.e., associated at only chance levels, the pattern of occurrence of symptoms profiles will be fitted by the standard model of independence. In this case, each symptom occurs at a particular rate in the sample as a whole, and there is no reason to suspect that these symptoms identify an underlying classification (i.e., that there are different types of patients). However, if the symptoms are not independent, one may propose that their pattern of occurrence can be explained by a single latent classification (present or absent) of which each symptom is indicative. If this is the case, the data will be fitted by the basic latent class model: each symptom occurs at a particular rate within each class, but the rates differ across classes. The parameters of the model indicate the relative frequencies of the latent diagnostic classes and the probability that each symptom is present within each of the latent diagnostic classes. Symptoms which discriminate well will exhibit a substantially greater probability of being present in the endogenous class than in the non-endogenous class. Golden (1982) has suggested a criterion of a difference of $d = 0.20$ or greater for a symptom to be meaningfully included as an indicator but for our analyses, we adopted a less strict criterion of 0.15, so as not to drop any symptom prematurely.

If the basic latent class model fits the data, specific relationships between the diagnostic classes and the symptoms (e.g., that the presence of a symptom is necessary and/or sufficient to make the diagnosis) can be tested by fixing (restricting) the values of appropriate model parameters. It should be noted that the fit of such a restricted model will be equal to, or worse than, that of the unrestricted model, since it tests whether both the model and the restrictions are true. If the goodness-of-fit of the two models is not significantly different, the restricted model is supported, but if the unrestricted model fits significantly better, it provides a more likely basis for diagnostic classification.

Whether a particular model fits the observed clinical data is tested using standard model testing procedures. Empirical data are employed to estimate the parameter values, and the expected frequency of each symptom profile is computed. These are then compared to the observed frequencies, using chi-square procedures. If the model is not rejected, it is tentatively accepted. How well the model describes the data can be evaluated by observing the size of the chi-square statistic, whose expected value under the model is equal to the degrees of freedom. The relative fits of nested alternative models can also be tested, with the difference in the likelihood ratio chi-square statistics of the two models being a chi-square statistic on the difference in their degrees of freedom (Goodman, 1970). Analyses were performed using the Maximum Likelihood Latent Structure Analysis programme (Clogg, 1977). Likelihood-ratio chi-squares are reported.

Results

The frequencies in the sample of the individual symptoms in the RDC endogenous and DSM–III melancholia criteria appear in Table I. The models of independence for all symptom sets considered did not fit the data ($P < 0.001$), indicating (as expected) that the symptoms considered were inter-related. Because it results in a clearer presentation, results of the analysis of the DSM-III melancholia criteria are presented first.

DSM–III melancholia

The first latent class model examined was that representing DSM–III melancholia criteria: eight symptoms are indicators of the presence or absence of the diagnosis, with pervasive loss of pleasure and lack of reactivity required. This model did not fit the data ($\chi^2 = 294.41$, df = 240 $P < 0.01$). Thus, these diagnostic criteria do not identify an underlying dichotomous classification of patients.

One potential explanation of this finding is that the symptoms are well chosen, but that the rule *requiring* the presence of the two specified symptoms is incorrect. This hypothesis can be tested by removing this restriction from the model. This unrestricted model fit the data adequately, although not exceptionally well ($\chi^2 = 263.05$, df = 238, $P = 0.13$). We can examine the relationship between the classification and each symptom by inspecting the difference in the probability that a symptom is present within each class. Pervasive loss of pleasure ($d = 0.54$) and lack of reactivity ($d = 0.50$) were strong indicators; terminal insomnia ($d = 0.26$), and decreased appetite or weight loss ($d = 0.25$) were weaker indicators. Distinct quality of mood ($d = 0.14$), guilt ($d = 0.09$), and worse in the morning ($d = 0.06$) were poor indicators. Marked psychomotor dysfunction ($d = 0.12$) also failed this test, but, given its low rate of occurrence in the sample (11·8%), its discriminating power was nearly as large as was possible. When it was present it was a strong indicator, but its absence signified little.

We, therefore, tentatively left marked psychomotor dysfunction in the model, while dropping the three poor indicators, and re-analysed the unrestricted model with only the remaining five symptoms. This model did not fit

TABLE II

Estimated parameter values for melancholia analyses: anhedonic and vegetative sub-typing variables

Symptom	*Sub-type*	*Probability symptom present in sub-type*	
		Model IV	*Model V*
Loss of pleasure	Non-anhedonic	0.274	0.243
	Anhedonic	0.862	0.861
Lack of reactivity	Non-anhedonic	0.127	0.112
	Anhedonic	0.636	0.631
Terminal insomnia	Non-vegetative	0.362	0.338
	Vegetative	0.811	0.751
Appetite or weight loss	Non-vegetative	0.554	0.484
	Vegetative	0.940	0.926
Psychomotor dysfunction	Non-anhedonic	0.034	0.039
	Anhedonic	0.147	0.142
	Non-vegetative	0.062	0.053
	Vegetative	0.195	0.166
Distinct quality	Non-anhedonic	0.600	0.587
	Anhedonic	0.752	0.754
	Non-vegetative	0.717	—
	Vegetative	0.712	—
Guilt	Non-anhedonic	0.692	—
	Anhedonic	0.786	—
	Non-vegetative	0.725	—
	Vegetative	0.805	—
Worse in the morning	Non-anhedonic	0.354	—
	Anhedonic	0.385	—
	Non-vegetative	0.362	—
	Vegetative	0.398	—
		Latent sub-type proportions	
	Neither	0.216	0.180
	Vegetative only	0.033	0.055
	Anhedonic only	0.313	0.250
	Both	0.438	0.516

the data ($\chi^2 = 36.33$, df $= 20$, $P < 0.025$)—a result which was somewhat surprising, since we had expected an improved classification by eliminating some of the 'noise' in the system. The parameter values in the two models were very similar, indicating that dropping the three symptoms did not reorganise the latent construct. By eliminating some 'noise', a dichotomous classification based on melancholia symptoms, which at first appeared marginally acceptable, had to be rejected.

This result is inconsistent with the hypothesis of a simple melancholic-non-melancholic sub-typing of depression. However, we did observe that these 'melancholia' symptoms were inter-related. Is there some sub-typing of patients which can explain these relationships? In order to generate a new hypothesis, we examined all the two-way relationships between the eight melancholia symptoms, using a log-linear analysis ($\chi^2 = 208.95$, df $= 219$). The effect parameters for eight of the 28 two-way relationships were significant ($P < 0.05$), which is fewer than one would expect if these eight symptoms jointly indicated a simple dichotomous classification. The magnitudes of the effects for the relationships between (1) pervasive loss of pleasure and lack of reactivity, and (2) decreased appetite or weight loss and terminal insomnia were twice as large as those of the other significant effects. Other symptoms were more weakly related to these groups of symptom. This suggested that there may be *two* dichotomous sub-typing variables, which we will label 'anhedonic/non-anhedonic' and 'vegetative/non-vegetative' respectively.

This new hypothesis was tested by considering a latent class model with all eight symptoms and *two* dichotomous (absent/present) latent variables. Pervasive loss of pleasure

TABLE III

Estimated parameter values for endogenous analyses: Anhedonic and vegetative sub-typing variables

Symptom	*Sub-type*	*Probability symptom present in sub-type* *Model VIII*	*Model IX*
Loss of pleasure	Non-anhedonic	0.233	0.145
	Anhedonic	0.886	0.884
Lack of reactivity	Non-anhedonic	0.150	0.142
	Anhedonic	0.627	0.609
Middle or terminal insomnia	Non-vegetative	0.636	0.630
	Vegetative	0.818	0.814
Appetite loss	Non-vegetative	0.249	0.211
	Vegetative	0.999	0.988
Weight loss	Non-vegetative	0.112	0.095
	Vegetative	0.746	0.727
Psychomotor dysfunction	Non-anhedonic	0.606	—
	Anhedonic	0.694	—
	Non-vegetative	0.591	—
	Vegetative	0.618	—
Distinct quality	Non-anhedonic	0.596	0.597
	Anhedonic	0.760	0.754
	Non-vegetative	0.735	—
	Vegetative	0.710	—
Guilt	Non-anhedonic	0.703	—
	Anhedonic	0.780	—
	Non-vegetative	0.758	—
	Vegetative	0.763	—
Worse in the morning	Non-anhedonic	0.307	—
	Anhedonic	0.384	—
	Non-vegetative	0.349	—
	Vegetative	0.375	—
		Latent sub-type proportions	
	Neither	0.154	0.128
	Vegetative ony	0.095	0.089
	Anhedonic only	0.242	0.240
	Both	0.509	0.543

and lack of reactivity were directly related only to the anhedonic variable; decreased appetite or weight loss and terminal insomnia were directly related only to the vegetative variable. The other symptoms were left unrestricted and their relationships to the sub-types were freely estimated. This model fitted the data extremely well ($\chi^2=227.16$, df$=230$).

The estimated parameter values for the model of two sub-typing variables appear in Table II (Model IV). As expected, pervasive loss of pleasure ($d=0.59$) and lack of reactivity ($d=0.51$) were strong indicators of the anhedonic sub-type; terminal insomnia ($d=0.45$) and decreased appetite or weight loss ($d=0.39$) were strong indicators of the vegetative sub-type. Again, guilt ($d=0.09$ and 0.08, respectively), and worse in the morning ($d=0.03$ and 0.04, respectively) were poor indicators, in this case of both anhedonic and vegetative sub-types. Distinct quality again was a poor indicator of the vegetative sub-types ($d=-0.005$), but just met the criterion as an indicator of the anhedonic sub-type ($d=0.15$). Marked psychomotor dysfunction continued to be as strong an indicator as could be expected, given its low rate of occurrence. It was related approximately equally to both the anhedonic ($d=0.11$) and the vegetative ($d=0.12$) sub-types.

Based on these results, we removed the two poor indicators from the model, tentatively retaining distinct quality, related to the anhedonic sub-type only, and marked psychomotor dysfunction. This new six-symptom model fitted the data well ($\chi^2=54.08$ df$=46$), and the estimated parameter values from it appear in Table II (Model V). The estimated proportion of patients in each of the 2×2 classification was as follows: both sub-types absent, 18.0%; anhedonic only, 25.0%; vegetative only, 5.5%; anhedonic and vegetative, 51.6%. Note that the anhedonic sub-type occurred without the vegetative, but that the vegetative occurred only rarely in patients without the anhedonic sub-type.

RDC endogenous

These analyses largely parallel those just presented for melancholia. Although the requirement of at least one of the symptoms in group A of the RDC criteria (Table I) cannot be built into the model directly, this is a special case of the models being considered, and cannot be supported

TABLE IV
Estimated parameter values for synthesis analyses: Anhedonic and vegetative sub-typing variables

Symptom	*Sub-type*	*Probability symptom present in sub-type*	
		Model X	*Model XII*
Loss of pleasure	Non-anhedonic	0.254	0.220
	Anhedonic	0.878	0.895
Lack of reactivity	Non-anhedonic	0.130	0.167
	Anhedonic	0.632	0.624
Insomnia:			
Middle only	Non-vegetative	0.268	—
	Vegetative	0.110	—
Terminal	Non-vegetative	0.331	0.350
	Vegetative	0.740	0.713
Appetite-weight:			
Decreased appetite only	Non-vegetative	0.224	—
	Vegetative	0.253	—
Weight loss	Non-vegetative	0.272	0.256
	Vegetative	0.653	0.649
Distinct quality of mood	Non-anhedonic	—	0.604
	Anhedonic	—	0.759
		Latent sub-type proportions	
	Neither	0.197	0.205
	Vegetative only	0.051	0.050
	Anhedonic only	0.218	0.188
	Both	0.534	0.558

unless these more general models are supported. Also, only 23 subjects (3%) had no loss of pleasure. It was not possible to analyse the data meaningfully with such a small group, and we therefore collapsed the 'absent' and 'present but not pervasive' groups, yielding a dichotomous variable identical to that in the criteria for melancholia.

The first latent class model examined was that representing the RDC endogenous criteria; nine symptoms are indicators of the presence or absence of the diagnosis. This model fitted the data, although not particularly well ($\chi^2=518.52$, df=492, $P<0.20$). Examination of the parameter values revealed that five out of the nine symptoms were poor indicators: lack of reactivity (d=0.13), psychomotor dysfunction (d=0.13), distinct quality of mood (d=0.01), guilt (d=0.01), and worse in the morning (d=0.03). (Since the RDC do not require psychomotor dysfunction to be marked, a low base rate is not a problem in interpreting this analysis.) When these poor indicators were dropped, the new model fitted the data very well ($\chi^2=6.96$, df=6). However, loss of pleasure barely met the criterion to be retained in the model (d=0.15), and the remaining symptoms were all vegetative: decreased appetite (d=0.77), weight loss (d=0.64), and middle or terminal insomnia (d=0.18).

We therefore examined the hypothesis that, as in the melancholia analysis, *two* sub-typing variables exist; examination of the two-way relationships from a log-linear model including all two-way relationships ($\chi^2=420.48$, df=466) also suggested this structure. The same particularly strong relationships were observed between (a) loss of pleasure and lack of reactivity and (b) decreased appetite, weight loss, and middle or terminal insomnia. This hypothesis was tested by considering the latent class model with all nine symptoms and two dichotomous (absent/present) latent variables. Loss of pleasure and lack of reactivity were directly related only to the anhedonic variable; decreased appetite, weight loss and insomnia were related only to the vegetative variable; the four remaining symptoms were left unrestricted. This model fitted the data very well ($\chi^2=451.97$, df=482).

The estimated parameter values for this model appear in Table III (Model VIII). As expected, loss of pleasure (d=0.65) and lack of reactivity (d=0.48) were strong indicators of the anhedonic sub-type; appetite loss (d=0.75), weight loss (d=0.63) and middle or terminal insomnia (d=0.18) were indicators of the vegetative sub-type. Guilt, worse in the morning, and psychomotor dysfunction were very poor indicators of both the anhedonic sub-type (d=0.08, 0.08 and 0.09, respectively) and the vegetative sub-type (d=0.005, 0.03 and 0.03, respectively). Distinct quality of mood was a very poor indictor of the vegetative sub-type (d=0.025), but as in the melancholia analysis, just above the criterion level for the anhedonic sub-type (d=0.16).

Based on these results, we removed the three poor indicators from the model retaining distinct quality of mood as an indicator of the anhedonic sub-type only. This model fit the data well ($\chi^2=54.68$, df=48); the estimated parameter values appear in Table III (Model IX). The estimated proportion of patients in each of 2×2 classifications was quite similar to the results of the melancholia analysis: both sub-types absent, 12.8% anhedonic only, 24.0%; vegetative only, 8.9%; anhedonic and vegetative, 54.3%.

Synthesis

The results of the analyses of the criteria for endogenous and melancholic depression are highly congruent; this is not entirely surprising, since the symptoms they include overlap. However, there are differences in symptoms. In order to synthesise the results and to produce a working model with which to diagnose individual patients, we examined these differences from the point of view of their internal construct validity.

For sleep disturbance, criteria for melancholia count only terminal insomnia, while endogenous criteria accept either middle or terminal insomnia; we therefore created a sleep variable with three levels: neither, middle-only, terminal. The two criteria disagree on the significance of the middle-only level. For psychomotor dysfunction, melancholia criteria require the symptom to be marked, while endogenous criteria require it only to be present. We therefore created a three-level psychomotor variable: absent, present but not marked, marked. The two criteria disagree on the middle level. For loss of pleasure, melancholia criteria require the symptom to be pervasive, while the endogenous require it only to be present. However, only 23 patients in our sample (3%) had no loss of pleasure, and so they were collapsed to make a non-pervasive group; therefore we could not evaluate this difference between the two criteria.

Endogenous criteria treat decreased appetite and weight loss as two separate indicators, so that if both are present, two points are credited. Melancholia criteria treat them as one item, so that one point is credited, regardless of whether either one or both symptoms are present. Underlying the melancholia approach is the assumption that both decreased appetite and weight loss are indicative of a single 'appetite-weight' disturbance, which in turn is indicative of the sub-type. The correlation between decreased appetite and weight loss is due to their joint relationship to this appetite-weight disturbance, rather than to a separate relationship of each symptom to the sub-type. This structure can be represented by creating a single variable of the four combinations of appetite and weight loss. A model with this variable (the melancholic hypothesis) then can be contrasted to a model with the two symptoms as separate indicators (the endogenous hypothesis). In practice, weight loss without decreased appetite was observed in too few patients ($n=25$, 3.3%) to analyse meaningfully. Collapsing this group with that with both appetite and weight loss yielded three levels (neither, decreased appetite only, and weight loss with or without decreased appetite), and allowed us to examine decreased appetite unconfounded by weight loss.

At first, two models were evaluated. The first included decreased appetite and weight loss as separate variables, while the second included the three level appetite-weight variable. Both models included pervasive loss of pleasure, lack of reactivity, and the three level insomnia variable. (The more questionable indicators, quality of mood and psychomotor dysfunction, were not included at this stage, but were added after the issues regarding the more core symptoms were resolved.) As in the previous analyses, each of the symptoms was indicative of either the anhedonic or vegetative sub-types. Both models fitted the data very well ($\chi^2=37.61$, df=32 and $\chi^2=17.86$, df=20, respectively), and all the parameter values, other than those regarding decreased appetite and weight loss, were nearly identical. However, examining the parameters from the model with the three level appetite-weight loss variable (Table IV, Model X), we observed that decreased appetite alone was a very poor indicator of the vegetative sub-type (d=0.03). Weight loss, however, was a strong indicator (d=0.38). Thus, we concluded that the apparent effect of decreased appetite, when considered separately, was spurious, due to its correlation with weight loss.

Further examination of the parameters of this model indicated that middle insomnia only was a poor indicator of the vegetative sub-type, and was actually more likely in *non*-vegetative patients (d=−0.16). Terminal insomnia, on the other hand, was a strong indicator (d=0.41). Thus, the apparent effect of "middle or terminal insomnia" was due to terminal insomnia and to any correlation between middle and terminal insomnia.

Given these results, we examined a model with weight loss, terminal insomnia, pervasive loss of pleasure, and lack of reactivity, and added to it the two more ambiguous symptoms of psychomotor dysfunction (three levels) and distinct quality of mood (related to anhedonia only). This model fitted the data, although not well ($\chi^2=92.52$, df=74, $P<0.07$). Distinct quality of mood continued to be a marginally acceptable indicator of the anhedonic subtype (d=0.15) and was retained. Less than marked psychomotor dysfunction was a poor indicator of both the anhedonic (d=0.004) and the vegetative sub-type (d=0.08); marked psychomotor dysfunction was a somewhat stronger indicator for both the anhedonic sub-type (d=0.10) and the vegetative sub-type (d=0.12). However, the probability of marked psychomotor dysfunction being present was increased only when *both* the anhedonic and vegetative subtypes were present. These probabilities were 0.04, 0.08, 0.05 and 0.18 for neither sub-type, vegetative only, anhedonic only, and both sub-types respectively. Since this symptom did not appear to be a direct indicator of either sub-type, we removed it from the model; this had little effect on the value of the other parameters.

This final model included weight loss, terminal insomnia, distinct quality of mood, pervasive loss of pleasure, and lack of reactivity, and fitted the data extremely well ($\chi^2=17.68$, df=18). The estimated parameter values appear in Table IV (Model XII); as in the endogenous and melancholia analyses, the vegetative subtype rarely occurred without the anhedonic sub-type (5% of the sample).

In order to test the robustness of this final model, we performed a split-half procedure: the sample was split in half randomly, and a "group" variable was added to the model (Clogg & Goodman, 1984). The classification structure of Model XII was applied to both groups. First, the parameters were allowed to take different values in the two groups, to determine whether this structure fitted the two samples; results indicated an excellent fit ($\chi^2=38.85$, df=36). Next, the parameter values were restricted to be equal across groups; this makes the assumption that there is one population with a single set of parameters which are estimated by the pooled estimates and that differences across groups are due to sampling error. The non-significant difference between the χ^2 from these two models indicated support for this hypothesis ($\chi^2=9.65$, df=13). In addition, 12 of the 14 independent pooled estimates fell between the split-half estimates; the two which did not differed from their closest split-half estimate by less than 2%. Results indicated that the two samples were both well described by the model and that the parameter values were not significantly different in the two groups.

Individual patients can be assigned to the sub-types by calculating the probability of being in each, for each five-symptom profile. Examination of these values suggested the following approximate algorithms. Patients are classified as anhedonic if they have pervasive loss of pleasure, or both lack of reactivity and distinct quality of mood. Since the vegetative sub-type is related to the anhedonic sub-type, in that it rarely occurs without it, its diagnosis will depend on the presence or absence of the anhedonic sub-type, as well as the presence of the vegetative symptoms. The results suggested that patients be classified as vegetative if: (a) they are anhedonic (by the above criteria) and have either weight loss or terminal insomnia or (b) they are not anhedonic and have both weight loss and terminal insomnia. This algorithm represents somewhat of a compromise between the actual probabilities of the diagnoses obtained from the analysis and a desire for a simple algorithm. Further work is in progress to develop and refine the sub-typing criteria.

Discussion

The results presented here do not support the subtyping of major depression according to the RDC criteria for endogenous or the DSM-III criteria for melancholia. In fact, they indicate that the clinical features used in these criteria do not identify a single sub-typing. However, the data do suggest the existence of *two* sub-typing variables: an anhedonic subtype related to pervasive loss of pleasure, lack of reactivity, and distinct quality of mood; and a vegetative sub-type related to terminal insomnia and weight loss. This distinction between anhedonic and vegetative sub-types is supported by the preliminary finding of Hibbert *et al* (1984), that anhedonic and vegetative symptoms do not covary over time. While these findings are not consistent with the letter of the law of the RDC and the DSM-III they are consistent with their spirit. Both criteria are divided into two parts, representing two traditions in the symptomatic approach to 'endogenous' depression: the first parts deal primarily with anhedonic symptoms and the second with vegetative (as well as other) symptoms. Thus, both RDC and

DSM-III criteria could be interpreted as ineffectively selecting those patients who have both anhedonic and vegetative sub-types.

The anhedonic sub-type may correspond to the endogenomorphic depression presented by Klein (1974) or to the autonomous depression discussed by Nelson *et al,* (1980). The vegetative aspects of 'endogenous' depression also emerges as a distinct sub-type, but related to the anhedonic one, in that it rarely occurs in non-anhedonic patients. Our analysis also indicated that 20.5% of our sample was of neither the anhedonic nor the vegetative sub-type, but still met criteria for major depression; the identity and clinical significance of this group is also of interest. To the extent that this group can be considered to consist of patients not considered to be 'endogenous' by any symptomatic approach, the sub-typing suggested here might be considered as an organizing of those patients never considered to be 'endogenous'.

Although decreased appetite and middle insomnia at first appeared to be good indicators of the vegetative sub-type, further study showed this to be spurious. While both may occur more frequently in vegetative patients, this is due to their associations with weight loss and terminal insomnia, respectively, and not to direct relationships with the sub-types. Psychomotor dysfunction was also unrelated to either sub-type, but marked psychomotor dysfunction occurred mostly in patients with both anhedonic and vegetative subtypes. Psychomotor dysfunction, especially retardation, has been considered a cardinal sign of 'endogenicity'; this may be because its presence also largely implies the presence of the anhedonic and vegetative sub-types as well. It is possible that patients who are both anhedonic and vegetative form a group with special significance with regard to aetiology, course, or treatment response.

Guilt and worse in the morning were also found to have no relationship to either sub-type. It may still be possible that these clinical features are related to the sub-types but that the SADS items do not measure them well. For example, guilt may need to be assessed more subtly than is done in a SADS interview; while the relevance of diurnal variation may not be limited to mood being worse in the morning or may be less common in severe depression (Waldman, 1972) and so not related to other variables in a simple fashion.

How do the results presented here relate to the series of a factor analytical and cluster analytical studies of the classification of depression which, in general, have found support for an 'endogenous' factor or cluster? In addition to providing an internally valid alternative sub-typing scheme, our results provide an explanation of those of these earlier studies. Given the hierarchical relationships among the anhedonic sub-type, the vegetative sub-type, and marked psychomotor dysfunction, it is not surprising that correlations between anhedonic and vegetative *symptoms* have been observed; these symptoms have been thought to identify a single sub-type. However, our results indicate that these correlations are indirect and due to the relationship between the two sub-types.

In addition, comparing the results of earlier studies to those presented here is not entirely straightforward. Firstly, the sub-typings found in any study will partially depend on the nature of the patient sample. In the present study, both in-patients and out-patients were included, although all were seeking treatment at major medical centres. Subjects recruited from less medically orientated clinics, or a sample with a greater representation of 'non-endogenous' patients, might present different symptom patterns and led to the derivation of additional or different sub-types. A less severely ill sample might also have allowed examination of loss of pleasure that is less than pervasive. Secondly, different studies have examined different, or only partially overlapping sets of symptoms. Of nine studies reviewed (Carney, *et al,* 1978; Kiloh & Garside, 1963; Rosenthal & Gudeman, 1967; Rosenthal & Klerman, 1966; Mendels & Cochrane, 1967; Paykel, 1971; Raskin & Crook, 1976; Andreasen, *et al,* 1980), all included terminal insomnia and eight included weight loss; but only six included lack of reactivity; four, loss of interest; and two, loss of appetite. Many studies also preceded the development of standardized interviews with much to collect symptom information reliably.

It also must be recognised that the different statistical methods employed examine different questions, and cannot be compared in a simple manner. Other authors (Maxwell, 1971; Kendell, 1975; Paykel, 1981) have noted the inappropriateness of factor analysis for the study of classification; in addition, both factor analysis (by definition) and cluster analysis (as most commonly applied) have been used to analyse symptoms scored on scales of increasing severity. Although the results of these studies may sometimes be discussed in terms of symptoms being present more frequently in particular groups, these analyses indicate whether symptoms are more or less *severe.* Whether defining depressive sub-types by the relative severity of symptoms is more appropriate, less appropriate, or doing something conceptually different is an unanswered empirical question. However, the traditional approach has been to consider the presence or absence of symptoms as indicative of the presence or absence of the diagnosis. This kind of structure is represented by LCA, and thus the analyses presented here evaluate this kind of diagnostic formulation. Further, it should be noted that factor analysis (as employed) and cluster analysis (by definition) have been employed as exploratory techniques, in that the analyses incorporated no *a priori* hypotheses. In contrast, LCA tests and compares hypotheses regarding specific diagnostic structures. We note that the analyses presented here do not consider the possibility of 'endogenicity' being a dimension (Kendell, 1976; Eysenck, 1970), and that the results do not preclude the possibility of an 'endogenous' sub-type, based on other sets of symptoms or on non-symptom criteria (e.g., family history), if they do not produce associated syndromes of the symptoms which we have examined.

While our results suggest classifying individual patients on anhedonic and vegetative sub-types, the criteria derived for doing so are preliminary, and must be used with caution. Additional symptom-indicators, and/or refinement in definition and assessment of symptoms may yield improved diagnostic criteria for these sub-types. Studies of external validation are also necessary to demonstrate their external validity and clinical usefulness. The analyses presented here are an attempt to clarify the relationships between traditionally 'endogenous' clinical features and the depressive sub-types they might identify. As a result, attempts to correlate combinations of anhedonic and vegetative sub-types with variables such as personality measures, family psychiatric history, course, and treatment response may be more successful than have been previous attempts to do so with the endogenous sub-type.

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*Michael A. Young PhD, *Assistant Professor, Departments of Psychiatry and Psychology. Rush-Presbyterian-St. Luke's Medical Center, Chicago, Illinois, 60612, USA.*

William A. Scheftner, MD, *Assistant Professor, Department of Psychiatry, Rush-Presbyterian-St Luke's Medical Center, Chicago, Illinois, 60612, USA.*

Gerald L. Klerman, MD, *Professor, Department of Psychiatry, Harvard Medical School, Boston, Massachusetts, USA.*

Nancy C. Andreasen, MD, PhD, *Associate Professor, Department of Psychiatry, University of Iowa College of Medicine, Iowa City, Iowa, USA.*

Robert M. A. Hirschfeld, MD, *Chief, Center for Studies of Affective Disorders, Clinical Research Branch, Division of Extramural Research Programs, National Institute of Mental Health, Rockville, Maryland, U.S.A.*

From the National Institute of Mental Health, Clinical Research Branch, Collaborative Program on the Psychobiology of Depression: Clinical Studies

*Correspondence

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The Depressive Symptoms of Bulimia Nervosa

PETER J. COOPER and CHRISTOPHER G. FAIRBURN

Standardised measures of mental state were used to compare patients with bulimia nervosa with those with major depressive disorder. The two groups were found to be similar in terms of severity of psychiatric disturbance, as measured by the Montgomery & Åsberg Scale and the Present State Examination. Noteworthy symptomatic differences were a greater frequency of obsessional ruminations and anxiety amongst the first group, and a greater frequency of depressed mood, apparent sadness, and suicidal ideation amongst the second. Discriminant function analyses revealed that the two patient groups had a different pattern of symptoms. Examination of the character of the psychiatric symptoms of patients with bulimia nervosa suggests that the anxiety and depressive symptoms are likely to be secondary to the eating disorder itself, rather than of primary significance.

Bulimia nervosa (BN) is an eating disorder in which a profound and distressing loss of control over eating results in episodes of bulimia (Russell, 1979; Fairburn, 1983). Body weight usually lies within the normal range due to a variety of compensatory behaviour, including self-induced vomiting, purgative abuse and extreme dieting. Accompanying the behavioural disturbance are grossly abnormal attitudes to body shape and weight and to food and eating, as well as a wide range of neurotic symptoms (Fairburn & Cooper, 1984a).

Bulimia nervosa appears to be a common disorder (Fairburn & Cooper, 1982; Fairburn & Cooper, 1984b). A recent survey of young adult women found that its prevalence was 1–2% (Cooper & Fairburn, 1983). In the United States a similar syndrome—'bulimia'—is included in DSM III (American Psychiatric Association, 1980); and it has a prevalence rate similar to that of BN (Pyle *et al*, 1983).

Four lines of evidence have been used to argue that the syndrome bulimia is 'closely related to' or 'a form of' major affective disorder (Hudson *et al*, 1983a, 1984). Firstly, depressive symptoms are common amongst patients with bulimia (Pyle *et al*, 1981). Secondly, family history studies have revealed a high prevalence of affective disorder amongst these patients' relatives (Hudson *et al*, 1983b). Thirdly, tests of neuroendocrine function, such as the dexamethasone suppression test, have shown similarities between these patients and those with affective disorder (Hudson *et al*, 1983a). Lastly, it has been reported that patients with bulimia respond to treatment with antidepressant drugs (Pope *et al*, 1983; Walsh *et al*, 1982). While each of these lines of evidence is open to question, if it were confirmed that bulimia is closely related to the affective disorders, this would have major implications for our understanding of the condition.

This paper is concerned with the first line of evidence; i.e. the character of depressive symptoms of patients with BN. Whilst it has been noted (Russell, 1979; Pyle *et al*, 1981; Fairburn, 1983) that depressive symptoms are common amongst these patients, there have been no systematic phenomenological studies. The aim of the present investigation was to describe the depressive symptoms of a sample of these patients using well-established assessment instruments, and to compare their symptoms with those of patients with major depressive disorder.

Method

The cases of bulimia nervosa

A letter was sent to all general practitioners in the Oxford area requesting the referral of patients for possible inclusion in a study of the treatment of BN. They were asked to refer patients aged over 17 years who complained of having lost control over eating and who used self-induced vomiting as a means of compensating for overeating. Local psychiatrists also agreed to refer all such patients.

Patients were asked to attend for a two hour assessment interview to elicit biographical data together with information for a clinical diagnosis; and a standardised assessment of mental state was made by an experienced research assistant who had been trained in the use of the various measures. Each interview was tape-recorded. Patients also completed certain self-report questionnaires.

The diagnosis of bulimia nervosa

A strict operational definition of bulimia nervosa was used, based on the diagnostic criteria of Russell (1979):

(i) The patient had to deny having control over her eating and report having experienced at least four episodes of bulimia or 'binge-eating' over the previous four weeks, as well as an average of at least one binge a week over the previous six months. The following definition of a binge was given: 'We use the term binge to refer to episodes of uncontrolled eating in which a huge amount of food is consumed, often rapidly and in secret. These episodes usually end because of stomach pain, interruption by others, running out of food supplies, or vomiting. Although the actual eating may be enjoyable, afterwards one invariably feels disgusted, guilty and depressed'.

(ii) The patient had to report having made herself sick on at least four occasions over the past four weeks, and on average, at least once a week over the previous six months. On each occasion, the vomiting had to be induced rather than spontaneous, and be performed either as a method of weight control or to compensate for having overeaten, or both. Patients who did not practice self-induced vomiting were excluded. Thus, this definition of BN is somewhat narrower than Russell's, since it did not include people who use purgatives rather than vomiting as a means of weight control.

(iii) The patient had to exhibit psychopathology suggestive of a morbid fear of fatness (see Fairburn & Cooper, 1984a, for the operational definition).

(iv) The patient had to weigh at least 80% of the matched population mean weight (MPMW) (Geigy, 1962).

Measures

Specific psychopathology: A semi-structured pre-coded interview was used to assess the psychopathology characteristic of patients with BN. The major items were: fear of fatness, pursuit of weight loss, sensitivity to weight gain, body image disparagement, binge-eating, self-induced vomiting, use of purgatives or exercise for weight control, frequency of weighing, desired weight, anxiety in eating-related situations, and the avoidance of such situations.

In addition to the interview, two self-report questionnaires were used to assess the specific psychopathology: the Eating Attitudes Test (EAT) (Garner & Garfinkel, 1979), a measure of abnormal eating habits and abnormal attitudes to food, eating, body weight and shape (Button & Whitehouse, 1981; Garner *et al*, 1982); and the Three Factor Eating Questionnaire (Stunkard & Messick, 1981), from which a measure of 'dietary restraint' was derived.

Non-specific psychopathology: The principal measures were as follows:
(a) The Present State Examination (PSE) (Wing *et al*, 1974), a standardised interview for assessing the presence or absence of symptoms within the neuroses and functional psychoses. (b) The Montgomery & Åsberg Depression Rating Scale (MADRS) (Montgomery & Åsberg, 1979), a sensitive measure of depression.

An assessment was made of the inter-rater reliability of the MADRS and PSE data. All interviews were tape-recorded and a random sample of one in four rated by an experienced independent assessor. The correlation (Pearson r) for the individual MADRS items ranged from 0.45 to 1.00; and for the MADRS total score there was almost perfect agreement ($r = 0.97$). A similar high correlation was obtained for the PSE total score ($r = 0.96$), and the agreement between the two raters on the presence or absence of each PSE symptom was equally good. For 11 PSE symptoms there was perfect agreement that the symptom was either present or absent. For the remainder the mean kappa was 0.94 (range 0.60 to 1.00).

This paper is concerned with the non-specific psychopathology of the patients; their overall clinical characteristics and specific psychopathology have been described elsewhere (Fairburn & Cooper, 1984a).

The cases of major depressive disorder

A colleague (Dr. J. Teasdale) requested all Oxfordshire general practitioners to refer for possible inclusion in a study of cognitive therapy for depression patients between the ages of 16 and 60 with a score of over 20 on the Beck Depression Inventory (Beck *et al*, 1961). These were assessed by a psychiatrist using the Present State Examination (Wing *et al*, 1974), the Hamilton Rating Scale for Depression (HRSD) (Hamilton, 1960), and the MADRS. Patients who fulfilled Research Diagnostic Criteria for unipolar primary major depressive disorder (Spitzer *et al*, 1978) and scored 14 or more on the HDRS were considered eligible for inclusion in the study (Teasdale *et al*, 1984).

Results

The bulimia nervosa sample

Forty-six patients referred for treatment were sent an appointment, and all but three attended; 35 fulfilled the diagnostic criteria for BN. All also fulfilled DSM III criteria for the syndrome bulimia (American Psychiatric Association, 1980).

The primary major depressive disorder sample

Forty-four patients (40 of them women) were assessed and found to fulfil the selection criteria for major depressive disorder. Their age range was 23 to 59, ($\text{mean} = 37.9$, $\text{sd} = 10.0$), as compared with an age range of 18 to 35 for the BN sample ($\text{mean age} = 23.5$, $\text{sd} = 4.4$). The average ages of the two patient groups were significantly different ($t = 7.76$, $df = 73$, $P < 0.001$).

In order to determine whether age had a significant influence on mental state, the depressed patients were subdivided by means of a median split by age, and the two groups compared. The mean age of the younger group was 28.9 ($\text{sd} = 4.1$) which is close to that of the BN sample. There were no differences between the two age groups on the PSE in terms of the distribution of individual symptoms, syndromes, Index of Definition levels, or Catego classes; or on the MADRS in terms of mean total score or the mean scores for the individual MADRS items. It was therefore considered legitimate to use the full sample of depressed patients as a comparison group.

TABLE I

Mean scores on the Montgomery and Åsberg Depression Rating Scale for patients with bulimia nervosa and those with depression[1]

	Bulimia nervosa patients (*n* = 35)		Depressed patients (*n* = 40)		
	x	sd	x	sd	t
Apparent sadness	1.40	1.19	3.03	1.25	5.66**
Reported sadness	3.31	0.90	3.25	1.06	0.08
Inner tension	3.00	0.84	2.35	0.70	3.61**
Reduced sleep	2.44	1.56	3.25	1.50	2.26*
Concentration difficulties	3.40	1.12	3.10	1.24	1.08
Lassitude	2.94	1.68	2.38	1.17	1.45
Inability to feel	2.26	1.48	2.40	1.01	0.48
Pessimistic thoughts	3.63	0.77	2.25	1.06	4.41**
Suicidal thoughts	1.86	1.59	3.03	1.25	3.51**
MADRS total	26.40	8.53	26.05	6.34	0.20

* $P<0.05$

** $P<0.001$

[1] The MADRS item of Reduced Appetite is not included in the table in view of the difficulty in rating this item in patients with eating disorders. The MADRS total score for the bulimia nervosa cases was accordingly pro-rated for comparison with the depressed patients.

Severity of depressive symptoms

(i) *Montgomery & Åsberg Depression Rating Scale*

Table I shows a comparison of the MADRS scores of the two groups. In terms of overall severity, the two samples were similar: indeed, the mean total MADRS scores were virtually identical, but the two groups differed on certain items. Compared with the patients with BN, those with primary depression had significantly higher scores on 'apparent sadness', 'reduced sleep' and 'suicidal thoughts'; and significantly lower scores on 'inner tension' and 'pessimistic thoughts'.

(ii) *Present State Examination*

The mean total PSE score (i.e. mean aggregate of the symptoms scores) was similar for the two groups: 22.4 (sd = 10.1) for those with BN, and 22.5 (sd = 7.2) for those with primary depression (t = 0.04, NS). However, there were marked differences between the groups in terms of the mean aggregate scores for the three non-psychotic PSE depressive syndromes. Compared with the patients with BN, those with primary depression had significantly higher mean scores for 'simple depression' (t = 3.56, df = 73, $P<0.001$) and 'other (somatic) features of depression' (t = 3.43, df = 73, $P<0.001$); and a significantly lower mean score for 'special features of depression' (t = 4.48, df = 73, $P<0.001$).

Description of mental state

(i) *PSE Index of Definition (ID) and Catego classes*

Twenty-eight (80%) of the 35 patients with BN had an ID of 5 or more and were therefore 'PSE cases'. All the patients with major depressive disorder were 'PSE cases'. Amongst the BN PSE-ID cases, 75% had an ID above 5 as compared with 63% of the depressed patients.

There was a major difference between the two patient populations in terms of the distribution of Catego classes. Amongst those with depression, 92.5% had a Catego class of N or R (i.e. neurotic or retarded depression); and 7.5% a Catego class of M (i.e. mania). Amongst the 28 BN PSE cases, 18 (64.3%) had a Catego class of N or R; nine (32.1%) had a class of M; and one (3.6%) had a class of A (i.e. anxiety).

(ii) *PSE syndromes*

Table II shows the frequency of PSE syndromes amongst the two patient populations. 'Simple depression' was the only syndrome present in a significantly greater proportion of those with depression than those with BN. Four syndromes were significantly more common amongst those with BN: 'obsessional neurosis', 'situational anxiety', 'hypomania', and 'special features of depression'.

(iii) *PSE symptoms*

When the PSE symptoms were arranged in descending order of frequency for the patients with BN, the two groups differed significantly on 12 of the 42 symptoms. Those more common amongst the patients with depression were 'depressed mood', 'social withdrawal', 'loss of interest', 'loss of libido', 'tension pains' and 'suicidal plans or acts'; and those more common amongst the patients with BN were 'pathological guilt', 'obsessional ideas and ruminations', 'situational anxiety', 'autonomic anxiety on meeting people', 'expansive mood', and 'subjective ideomotor pressure'.

(iv) *PSE re-analyses*

In view of the difficulty rating the PSE symptoms of 'pathological guilt', 'elevated mood', and 'subjective ideomotor pressure' amongst patients with BN (vide infra), the PSE data of the BN sample were re-analysed with these three symptoms re-rated as absent. In terms of the number of ID cases, this made little difference: 25 as opposed to 28 were ID cases. However, the distribution of Catego classes changed considerably: of the 25 cases, three had a Catego class of A; and 22 had a class of N or R. The revised mean total PSE score was minimally reduced and still not different from that of the depressed patients. However, most of the differences between the two patient samples in terms of PSE syndromes disappeared: there was no difference between them in terms of mean total score on syndrome ED ('special features of depression'; t = 0.21, df = 73); nor in terms of the frequency of HM ('hypomania'; Fisher exact $P = 0.15$), or ED ('special features of depression', $X^2 = 0$, df = 1). The difference between the two groups of patients in terms of the frequency of SA ('situational anxiety') obviously remained.

Discriminant function analyses

Discriminant function analyses were conducted to deter-

TABLE II
Frequency of PSE syndromes amongst patients with bulimia nervosa and those with depression

Symbol	PSE syndrome	Bulimia nervosa patients ($n=35$) %	Depressed patients ($n=40$) %	χ^2
SD	Simple depression	62.9	100	15.5***
ON	Obsessional neurosis	80.0	20.0	24.6***
GA	General anxiety	48.6	60.0	0.4
SA	Situational anxiety	71.4	37.5	7.3**
HM	Hypomania	28.6	7.5	4.4*
DE	Depersonalisation	17.1	2.5	3.2
ED	Special features of depression	97.1	77.5	4.7*
IR	Ideas of reference	40.0	22.5	1.6
TE	Tension	77.1	95.0	3.7
LE	Lack of energy	71.4	75.0	0.0
WO	Worrying	94.3	100.0	0.7
IR	Irritability	74.3	85.0	0.8
SU	Social unease	88.6	92.5	0.0
IC	Loss of interest and concentration	82.9	97.5	3.2
HY	Hypochondriasis	0	7.5	1.1
OD	Other symptoms of depression	77.1	90.0	1.4

* $P<0.05$
** $P<0.01$
*** $P<0.001$

TABLE III
Standardised coefficients for the two discriminant functions

Analysis including all symptoms Symptom	Coefficient	*Analysis excluding five symptoms* Symptom	Coefficient
Pathological guilt	0.97	Obsessional ideas and ruminations	1.00
Obsessional ideas and ruminations	0.78	Depressed mood	−0.72
Depressed mood	−0.66	Tension pains	−0.63
Tension pains	−0.52	Guilty ideas of reference	0.44
Loss of interest	−0.38	Apparent sadness	−0.41
Subjective anergia and retardation	0.37	Loss of interest	−0.39
Obsessional checking and repeating	−0.34	Depersonalisation	0.35
Loss of libido	−0.30	Anxiety on meeting people	0.30
Nervous tension	−0.29	Suicidal plans or acts	−0.25
Subjective ideomotor pressure	0.23	Hypochondriasis	0.23

mine whether, in terms of symptoms alone, a natural boundary or discontinuity existed between patients with BN and those with depression. Initially, the data used were all the PSE symptoms, together with two items from the MADRS—'apparent sadness' and 'inability to feel', not included in the short version of the PSE. These variables were entered into a stepwise discriminant function analysis (Wilks' method). The best ten variables were chosen, preserving an adequate ratio of variables to subjects (Everitt, 1975), and the programme re-run by the direct method (Table III). The distribution of discriminant scores, shown in Figure 1, was examined for conformity to the normal distribution by Kolmogorov-Smirnov tests.

The discriminant function revealed a clear-cut bimodal distribution of scores (Fig. 1). There is only a small chance that this distribution could represent a normal distribution ($P=0.01$), and a high chance that the distribution for each of the two patient groups is normally distributed ($P=0.65$ for the patients with BN; $P=0.38$ for the patients with depression).

A second discriminant analysis excluded five problematic items: 'pathological guilt', 'hypomania', 'subjective ideomotor pressure', 'tiredness', and 'subjective anergia and retardation' (vide infra). The same method of analysis was used, and the top 10 variables are shown in Table III. The distribution of discriminant scores (Fig. 2), has a small chance of representing a normal distribution ($P=0.04$), and the probability that the distributions for the two patient groups are normally distributed is high ($P=0.78$ for the BN group and $P=0.58$ for the depressed group).

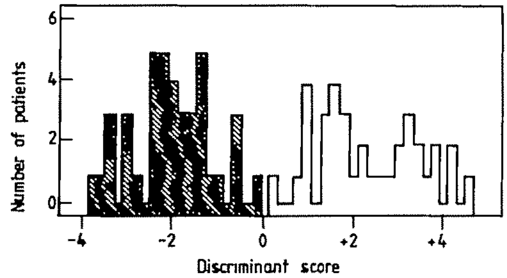

FIG. 1 Distribution of discriminant scores for patients with bulimia nervosa (unshaded) and those with depression (shaded), using all symptoms.

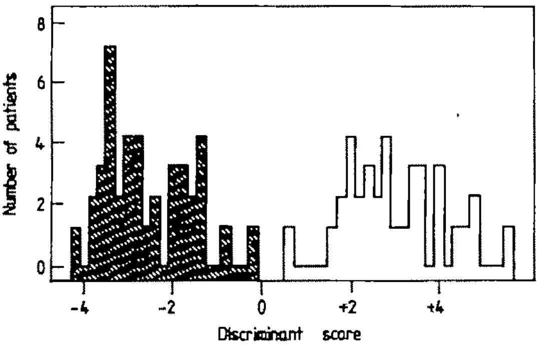

FIG. 2 Distribution of discriminant scores for patients with bulimia nervosa (unshaded) and those with depression (shaded), excluding five symptoms.

Discussion

It has been argued that the DSM III syndrome bulimia is 'closely related to' or 'a form of' major affective disorder (Hudson *et al*, 1983a, 1984), and this argument would apply equally to the equivalent syndrome of BN. One aspect of the argument concerns the prominence of depressive symptoms amongst this group of patients. The present paper provides the first systematic description of the frequency, nature and severity of depressive symptoms in BN. Standardised assessment measures of established validity and reliability were used to assess both depressive symptoms and other aspects of present mental state, the findings being compared with those obtained from a sample of patients with primary major depressive disorder. If BN were a form of affective disorder, it would be predicted that the two patient groups would have a similar mental state.

Certain difficulties emerged in using the PSE to describe the mental state of patients with BN. In particular, problems of definition arose in the rating of three symptoms: 'pathological guilt', 'expansive mood', and 'subjective ideomotor pressure'. When the PSE glossary definition of these symptoms was applied strictly, they were found to be present in 94%, 29% and 26% respectively. However, such figures are misleading since the character of these symptoms in patients with eating disorders is quite distinctive, and differs from the symptoms the PSE items are intended to describe. For example, the guilt was undoubtedly unpleasant, out of proportion, and beyond voluntary control; but in every case it related directly to the eating disorder; e.g. concerning minor dietary indiscretions such as the eating of 'forbidden' food. Some patients expressed guilt over years of secrecy and deceit, and it was common amongst those who shoplifted, but judged to be 'justifiable and appropriate'. 'Expansive mood' and 'subjective ideomotor pressure', were present in about a quarter of the BN sample and usually occurred together, but their time course was distinctive in that they rarely persisted for more than three or four hours, in contrast to these symptoms in patients without an eating disorder. Rating these three symptoms as present on the PSE led to several anomalous findings. For example, there was a high frequency of Catego class M; and high rates of the syndromes 'hypomania' and 'special features of depression'. Since these findings are open to question, the PSE was also analysed with these symptoms rated as absent.

In terms of mental state, the patients with BN resembled those with depression: they had equivalent mean total PSE and MADRS scores; and most PSE symptoms were present in an equal proportion of the two samples. However, there were some noteworthy differences. Compared with the depressed patients, those with BN had a significantly lower mean score on the MADRS item 'apparent sadness'. This highlights one of the difficulties in assessing patients with BN since, although they may not appear outwardly depressed, detailed assessment often reveals a variety of depressive symptoms. They had a lower mean score on the MADRS item 'suicidal thoughts'; and a lower frequency of the PSE symptom 'suicidal plans or acts', which conflicts with Russell's (1979) suggestion that patients with BN are at particularly high risk of suicide. Another important difference between the two groups of patients was that those with BN were more likely to report symptoms of anxiety, which were often severe and disabling, although usually attributable directly to the eating disorder itself. For example, the situational anxiety experienced by almost three-quarters of these patients was frequently related to social eating or being seen in public when 'feeling fat'.

The discriminant function analyses determined whether, despite their superficial similarities, the two groups of patients differed in terms of their overall mental state. The first analysis included all the variables, and the second excluded five PSE symptoms: the three mentioned earlier, together with 'tiredness' and 'subjective anergia'. It was judged that in many cases the latter two could be a direct consequence of the patients' disturbed eating, since three-quarters of them were inducing vomiting at least once daily; these five symptoms were rated as absent for both groups of patients, which minimised the chances of finding a non-normal distribution of discriminant scores.

A clear bimodality emerged from both these analyses. The symptom which contributed most to this was 'obsessional ideas and ruminations', rated as present in 80% of the patients with BN and in only 2.5% of the depressed patients. Amongst the former group, the ruminations invariably concerned food, eating, weight or shape. Although these thoughts undoubtedly fulfilled the PSE glossary criteria for obsessional ideas and ruminations, it could be argued that they were not truly obsessional phenomena since they were not stereotyped. For this reason, a further discriminant analysis was conducted in which this symptom and the five problematic items mentioned earlier were omitted. This analysis produced a distribution which was not so clearly bimodal. Ten variables produced a function which correctly classified just over 90% of cases: two (5.0%) of the depressed patients were incorrectly classified; and five (14.3%) of the patients with BN were incorrectly classified.

Given the similarity between the two populations of patients in terms of the severity of psychiatric disturbance, as measured by the PSE and the MADRS, the discontinuity which emerged from these analyses is striking. The relationship or inter-correlation between psychiatric symptoms seems to be different in patients with BN, compared with those with depression, casting doubt on the validity of the argument, based on phenomenology, that BN is a form of affective disorder. However, these observations need to be substantiated by cross-validating the present discriminant function on further groups of patients, and by generating new discriminant functions using further samples of patients with BN and with depression.

It is not possible to resolve complex nosological issues using cross-sectional phenomenological data of this type; information on response to treatment and on outcome are also required (Kendell, 1975). However this study has shown that the similarity between the mental state of patients with BN and those with depression is superficial, and that their pattern of symptoms is different. It also suggests that many of the depressive and anxiety symptoms of patients with BN are likely to be secondary to the eating disorder itself, rather than of primary significance. Longitudinal studies are required to confirm this impression. Our clinical experience, using psychological treatment, indicates that in the majority of cases of BN depressive and anxiety symptoms resolve in response to measures which enhance control over eating, although in a minority, antidepressant drugs are needed to treat a co-existing depressive disorder (Fairburn, 1982).

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*Peter J. Cooper, DPhil, DipPsych, *Lecturer in Psychopathology, Department of Psychiatry, University of Cambridge, Addenbrookes Hospital, Cambridge, CB2 2QQ.*

Christopher G. Fairburn, MA, MPhil, MRCPsych, *Wellcome Trust Senior Lecturer, Department of Psychiatry, University of Oxford, Warneford Hospital, Oxford OX3 7JX.*

*Correspondence

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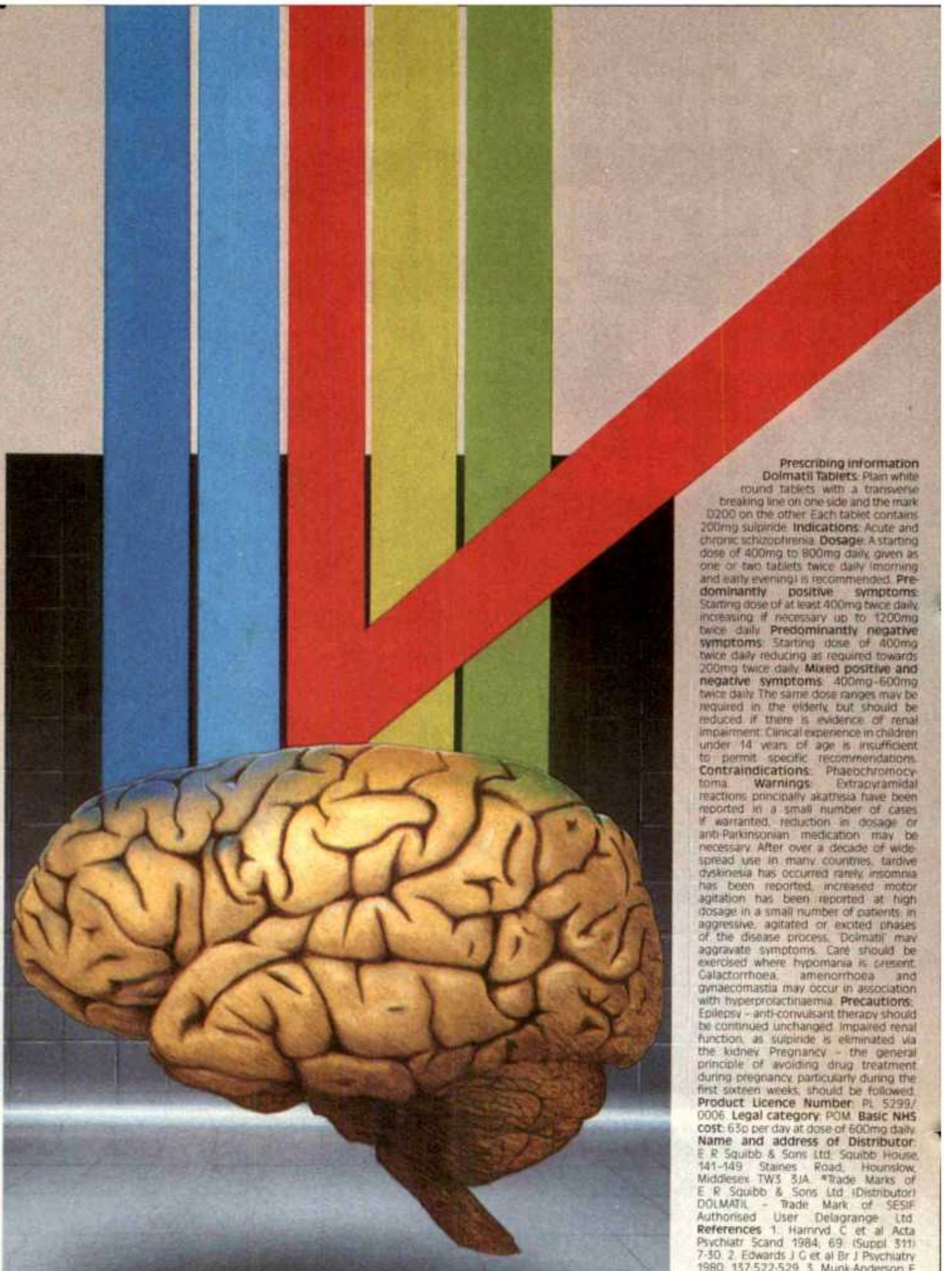

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British Journal of Psychiatry (1986), **148,** 275–278

The Diagnosis of Schizophrenia by Language Analysis

WILLIAM I. FRASER, KATHLEEN M. KING, PHILIP THOMAS and ROBERT E. KENDELL

Our aim was to test the findings of a study which claimed that, if the syntactic structure of schizophrenic speech were subjected to a detailed linguistic analysis, clear differences would be demonstrated between schizophrenic, manic and control populations. It was confirmed that schizophrenics do have less syntactically complex speech which contains more errors. Using linguistic variables in a discriminant function analysis, it was possible to predict diagnoses correctly in 79% of cases.

Psychotic speech often, but not always, seems strange. In the past decade psycholinguists have addressed the problem of analysis of psychotic language and raised the possibility of an objective linguistic test for schizophrenia. Reduced cohesion (or linking) in discourse has been utilised to identify schizophrenics with 73% overall accuracy by Rochester *et al* (1977). Hoffman *et al* (1982) claimed between 65% and 85% accuracy in the diagnosis of schizophrenia by deviations in propositions in texts.

Little attention was paid to the detailed syntactic analysis of schizophrenic speech until Morice & Ingram (1982) recently demonstrated that syntactic properties of psychotic and ordinary speech do differ, and can be used to discriminate schizophrenic, manic and non-patient control speakers with a diagnostic accuracy of 96%. These investigators collected speech samples from consecutive Australian patients with an admission diagnosis of schizophrenia ($n = 34$) or mania ($n = 11$) and carefully matched control speakers ($n = 18$). A linguistic profile of 118 variables was generated for each subject using an Apple II$_e$ microcomputer and a linguistic program package written specially for the project. These features of speech were measures of the complexity, variety, integrity and fluency of spoken language. The results of a discriminant function analysis suggested that the differences could be used diagnostically, subject to replication on a larger number of subjects. This is the report of an extended replication.

Method

The subjects in this study were consecutive admissions, aged between 16 and 65 years, to the Royal Edinburgh Hospital. They received the Present State Examination (PSE) (Wing *et al*, 1974) within twenty-four hours of admission and met the Research Diagnostic Criteria (Spitzer *et al*, 1975) for schizophrenia or mania derived from the PSE. Patients with organic brain syndromes were excluded, as were those with a primary casenote diagnosis of mental handicap, depressive illness, neurotic disturbance or personality disorder. Speech samples were collected from 30% of patients before they received any medication. Control subjects were selected from an outpatient physiotherapy clinic and were matched as closely as possible to the two patient groups for age, sex, educational standard attained, years of full-time education, social class and parental social class. English was the first language of all subjects and controls. The subjects of the initial study were 50 acute schizophrenics (defined as illness duration of less than five years) and 51 manic patients.

Free speech samples of a thousand words were recorded for each subject. As pilot studies suggested that Scots were more taciturn than Australians, the linguistic interview involved the presentation of standardised stimuli in the form of three simple cartoons before subjects were asked to talk about why they had come into hospital. In all other respects the procedure adhered to that of Morice and Ingram. Unpunctuated transcriptions were made from the tapes, sentence boundaries were created and manual grammatical analysis was performed by a trained research assistant with a coding manual based on the main standard reference of English grammar. (Quirk *et al*, 1972). Manual analysis was performed as a series of scans over each sentence, identifying low level dysfluencies such as repeated words and false starts, categorising each sentence as being well-formed or 'deviant' and, more importantly, constructing a syntax tree diagram for each analysable sentence. Each clause was identified as a marked node in the syntax tree, and detailed structural indices, verb phrase markings and dependent clause types were identified. In this way sentence complexity was identified. Interrater reliability between the Australian and Scots manual analysis was satisfactory on syntactic complexity, error and fluency variables. (Cronbach's alpha for mean depth of embedding, dysfluency index, and total error count were 0.93, 0.98 and 0.80, respectively).

All linguistic information from the manual analysis—the original texts, sentence classifications, dysfluencies, syntax trees and error identification—was transferred to

TABLE I
Demographic profiles of groups

		Schizophrenic (*n*=*50*)	*Manics* (*n*=*51*)	*Control* (*n*=*50*)
Sex	Male (*n*)	35	24	24
	Female (*n*)	15	27	26
Age	Mean (SD)	28.1 (8.98)	36.2 (13.48)	38.2 (14.17)
	Range	37	44	50
Years of education	Mean (SD)	12 (2.36)	12.9 (2.89)	11.8 (14.00)
	Range	8	8.4	14

floppy disc on an Apple IIe microcomputer in a form suitable for processing by a program package which was capable of recognising and counting various syntactic features and collating these into 118 measures of fluency, complexity and integrity. Data were analysed using the Statistical Package for the Social Sciences (Nie *et al*, 1975).

Results

These data (118 variables on 151 speech samples) were subjected to a factor analysis which, as in the Australian study, yielded separate complexity, error and fluency factors. As in the Australian study, the schizophrenics in the Scots study had the lowest scores on the major variables representing the complexity of speech (such as mean number of embedded clauses per complex sentence and mean depth of embedding). As regards speech errors, the Australian study suggested that schizophrenics had fewer well-formed sentences, more semantic and syntactic mistakes and a higher rate of dysfluencies (such as repeated words and false starts). The same was found for Scots schizophrenics.

Twenty-nine variables were selected for their ability to differentiate one of the three groups from the other two on a one-way analysis of variance at the 0.01 level and then were subjected to discriminant function analysis (DFA). The variables employed provided maximal separation between the groups on the basis of their scores on the two functions generated.

The constituent variables of Function 1 which discriminated controls from schizophrenics and manics were: % semantically deviant sentences, % well formed major sentences, total error count, % syntactically and semantically deviant sentences, no. of sentences with indeterminate clause structure, % syntactically deviant sentences, mean length utterance, no. of unclassifiable errors, % analysable sentences, no. of errors of grammatical insertion, mean length of utterance of analysable sentences, mean no. of major lexical items per analysable sentence, % indeterminate clause structure, % errors of omission, % sentences with embedding, mean maximum depth of embedding, mean no. of embedded clauses per complex sentence, mean no. of coordinated sentences (by other than 'and'), mean no. of coordinated top level clauses, no. of truncated sentences, and mean no. of clauses coordinated by 'and'. The constituent variables of Function 2 which discriminated manics from controls and schizophrenics were: % non-declarative sentences, no. of errors of tense or aspect, % pause fillers, % errors of commission, % exclamatory sentences, % dysfluencies, % verbs with two features marked, % repeat words, and dysfluency index.

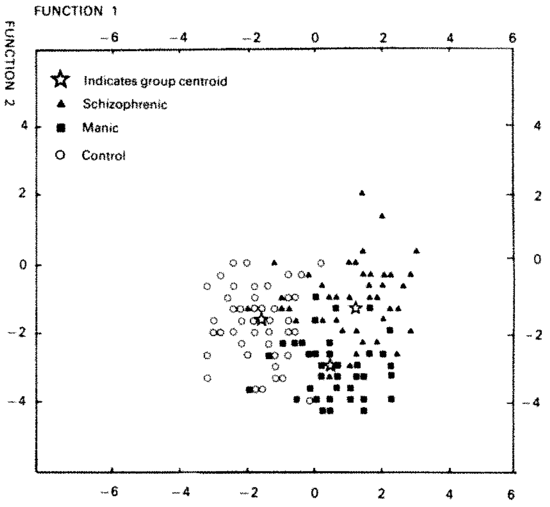

FIG. 1 Scatterplot of discriminant function scores for 50 schizophrenic (closed triangles), 51 manic (closed squares) and 50 control (open circles) subjects.

The manic group was the least unique of the three; only % of non-declarative sentences differentiated manics from both controls and schizophrenics at the 0.01 level. Each group was not individually characterisable; rather, there appeared to be a continuum of linguistic degeneration across the psychotic spectrum from controls, who produced fluent, complex and error-free utterances, to schizophrenics, who produced dysfluent, simple and error ridden speech.

TABLE II

Examples of differences in complexity, fluency and error variables in the schizophrenic, manic and control groups

Variable	*Schizophrenics (n=50)*		*Manic (n=51)*		*Control (n=50)*	
	Mean	*(SD)*	*Mean*	*(SD)*	*Mean*	*(SD)*
Mean depth of embedding (MDEMB)	1.30	(0.15)	1.31	(0.13)	1.39	(0.15)
Dysfluency index (DYSIN)	7.26	(3.74)	5.72	(2.88)	5.27	(2.21)
Total error count (ERR)	30.60	(17.12)	26.04	(13.21)	16.92	(8.67)

TABLE III

Classification table based on discriminant functions

Variables	*Classification*			
	Predicted	*Actual*		
		C	*M*	*S*
Australian DF				
Control	50	37	8	5
Manic	51	8	34	9
Schizophrenic	50	5	12	33
Scots DF				
Control	50	44	4	2
Manic	51	6	40	5
Schizophrenic	50	6	8	36

C = Control M = Manic S = Schizophrenic

Overall correct allocation: Australian DF = 68.2%; Scots DF = 79.5%

The mean scores of diagnostic groups on key variables of complexity, fluency and error types are shown in Table II.

Correlations significant at the $P<0.01$ level, were found between educational level (both years of completed full-time education and educational attainment) and indices of syntactic complexity, and between sex and integrity variables; females produced more fluent and grammatically accurate utterances.

The success of this DFA in distinguishing the groups is shown in Table III. Using the variables selected by the Australian discriminant analysis, 68.2% of Scots subjects were allocated to correct groups. Using our discriminant functions to classify our subjects back into their diagnostic groups we achieved 79.5% correct allocation. This higher correct allocation rate is partly due to the use of the same data to both generate and evaluate the discriminant function. The psychotic/non psychotic specificity was 0.79%, and sensitivity, 0.94%. Correct classification by chance would be 33.1% for schizophrenics and controls, and 33.8% for manics.

Discussion

In the past decade renewed attempts have been made to provide a descriptive account of psychotic language. We believe that the syntactic approach can discriminate among the speech of acute schizophrenics, manics and normal subjects. It is worth noting that the more exotic language productions of chronic schizophrenics were excluded from this study and will be described in a future report. Although our findings do not necessarily imply that psychotics have a primary language dysfunction, they do mean that psychotic illness is reflected in linguistic features which characterise the diagnostic groups.

The linguistic differences cannot be explained by medication effects. Among those on no drugs were some of the most speech-disordered. Hymowitz and Spohn (1980) have reported no decrease in complexity or coherence of speech due to phenothiazines.

Using a larger and dialectically different data base, the main findings of Morice and Ingram have been confirmed and a remarkably accurate diagnostic allocation rate has been achieved. This replication has theoretical and practical implications. The practical problems of developing a linguistically based diagnostic test, as suggested by Morice and Ingram, centre on the seven hours of parsing and data processing required *per patient*. The recent emergence of automated probablistic parsing may simplify this procedure sufficiently for linguistic analysis to be a feasible research tool. In particular, the emphasis should be on research into the correlates of these identified language abnormalities, and especially on how the course of the illness affects them.

Acknowledgements

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*William I Fraser, MD, FRCPsych, *Consultant Psychiatrist and Part-time Senior Lecturer, University Department of Psychiatry, Royal Edinburgh Hospital, Morningside Park, Edinburgh EH10 5HF.*

Kathleen King, MA, *Research Assistant, University Department of Psychiatry, Royal Edinburgh Hospital.*

Philip Thomas, MB, MPhil, MRCPsych, *Consultant Psychiatrist, Manchester Royal Infirmary, Hathersage Road, Manchester M13 9WL (formerly Lecturer in Psychiatry, Edinburgh University).*

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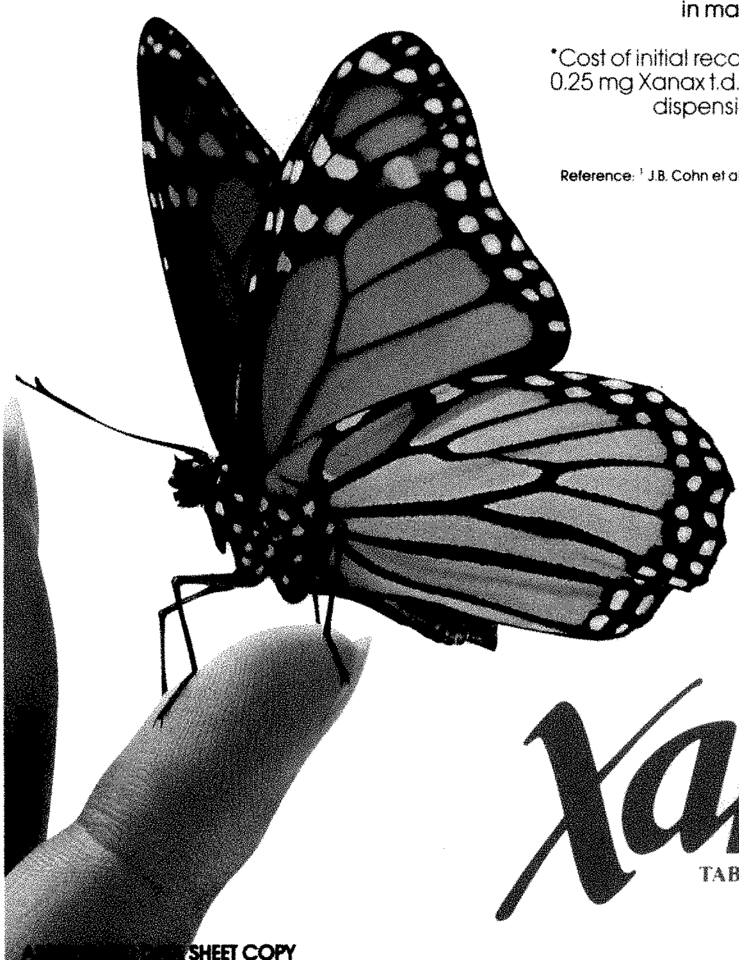

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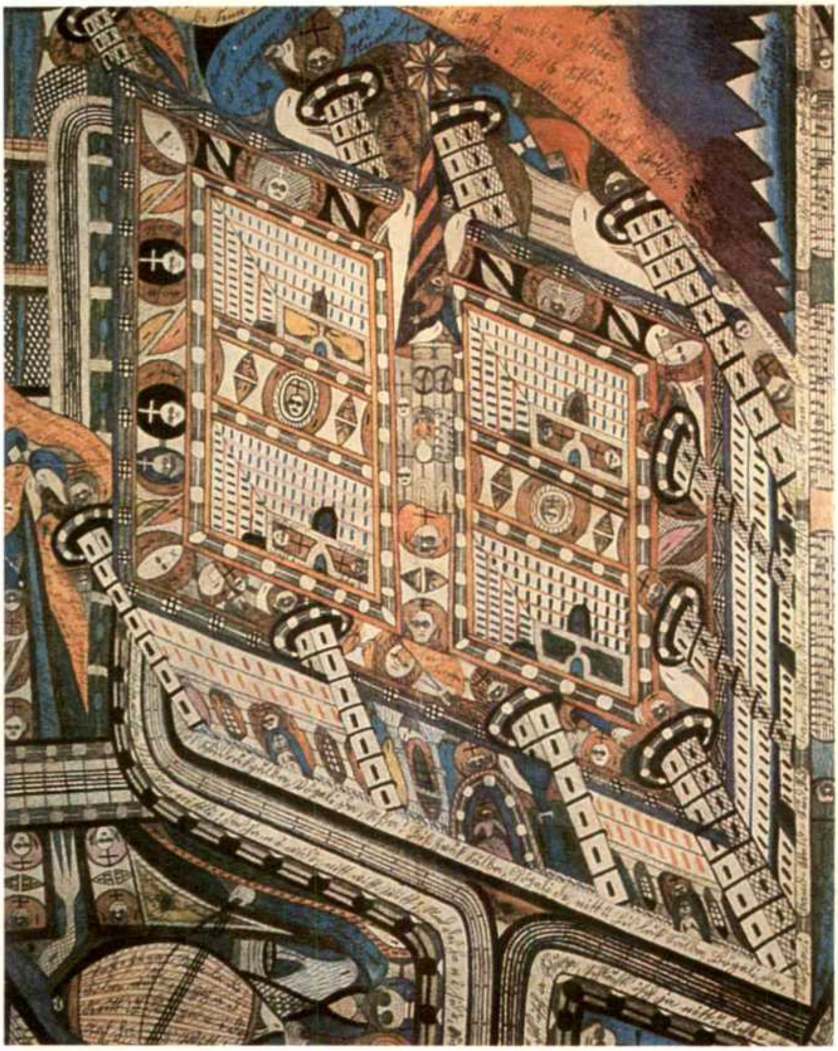

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trol is an indication for immediate
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6 months of therapy in those who
n most at risk. Hyperammonaemia
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lly transient, but may occasionally
ent clinically. If so Épilim should be
ontinued. Valproic acid inhibits platelet
egation. Thrombocytopenia has been
rted. Spontaneous bruising or bleeding
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British Journal of Psychiatry (1986), **148**, 279–287

The Impact of Individual and Family Treatment on the Affective Climate of Families of Schizophrenics

JERI A. DOANE, MICHAEL J. GOLDSTEIN, DAVID J. MIKLOWITZ and IAN R. H. FALLOON

Measures of parental affective style were compared for families of schizophrenics participating in a controlled treatment study which contrasted individual and family-based therapeutic programmes. The total number of critical statements and non-critical, intrusive remarks was significantly lower after three months for parents of schizophrenics participating in family therapy, compared to those whose offspring received only individual therapy. An increased risk for relapse was associated with an increase in the number of critical and/or intrusive remarks for patients in individual treatment. A significant increase in non-emotional, problem-solving statements was observed in parents who received family therapy, compared with those who did not. The results suggest that a behaviourally-oriented, problem-solving family approach may have reduced the risk of relapse in the first nine months after discharge from hospital by teaching families concrete ways of solving problems and concomitantly reducing the amount of negative emotional relating between family members.

In the past decade findings that the familial affective climate has an important influence on the course of illness for a schizophrenic family member have emerged (Brown *et al*, 1972; Vaughn & Leff, 1976a; Leff & Vaughn, 1981; Vaughn *et al*, 1982). These studies demonstrated that certain attitudes expressed by relatives towards a schizophrenic patient recently discharged from hospital, viz—highly critical and/or emotionally over-involved attitudes (expressed emotion or EE), lower the patient's threshold for subsequent relapse. These interactional behaviours, identified as psychotoxic, were fairly specific and involved styles of negative affective communication within the family. The Camberwell Family Interview (Vaughn & Leff, 1976b) was developed to measure EE; however, EE is not a measure of actual behaviour, but attitudes. Since attitudes and overt behaviour are not always isomorphic with one another, our team of investigators has carried out a series of studies that have attempted to assess the role of family affective climate in terms of behaviour, as it relates to the course of schizophrenia.

A measure of the family emotional climate reflecting actual verbal behaviour was developed by Doane *et al.* (1981). This coding system, Affective Style (AS), assesses several different kinds of affectively toned remarks made by the parent to the patient during actual face-to-face discussion. Thus, this measure is best viewed as an index of the relatives' affective *behaviour* toward the patient.

In a previous study of families of vulnerable non-psychotic adolescents (Doane *et al*, 1981), a profile method of grouping families on the AS measure was valuable in identifying cases among the sample whose initial disturbance subsequently deteriorated into major psychiatric disorder. This method involved grouping parents into negative or benign AS categories, according to whether or not they demonstrated certain low-frequency marker codes in direct interaction. Adolescent offspring of parents who used a negative AS marker code were more likely to develop a schizophrenia spectrum disorder five years later, while those from familes without this attribute had relatively good psychiatric outcomes.

In a recent study, this profile approach to grouping families was applied to a sample of schizophrenics in an effort to identify those at risk for early relapse (Doane *et al.*, 1985). The sample was comprised of 36 recently discharged patients, most of whom were from high-EE familes. The hypothesis was that among these high-EE homes, the most stressful, relapse-prone environments for the returning schizophrenic would be those in which the family interaction was characterised by a negative affective style. After an initial family assessment, patients were randomly assigned to either an individual or family therapy treatment programme. The family assessment was then repeated, three months after treatment had begun.

Families were assigned to one of three AS profile groups, based on the presence or absence of low-frequency, particularly harsh negative affective style behaviours expressed by parents. Results showed that after three months of the treatment, patients from families that had negative AS profiles were likely to relapse within the first nine months of treatment. This relationship was quite striking, but was true only for cases in the individual management treatment programme. Several cases in the family management programme also had negative family profiles at three months, but none of them relapsed. In fact, only one of the 11 relapses in the sample was in the family management programme. Clearly, the family treatment had a powerful effect on preventing relapse. Equally clear was that negative AS profiles were strongly associated with relapse in individually treated cases. What was unclear was why no relapse occurred in those family treatment cases where the therapy failed to change the negative AS profile.

We reasoned that perhaps something more subtle was changing in these families—some dimension of affective communication not captured in the family profiles. The AS profiles rely exclusively on the presence or absence of certain low-frequency marker codes. Perhaps a more global, broadly-defined measure of affective communication would be more sensitive in picking up subtle, yet perhaps meaningful changes occurring in the quality of affective verbal exchange in these families. In other words, perhaps family therapy helped reduce the global, 'atmospheric' dimension of intra-familial affective expression, thereby helping to diminish the probability of relapse.

To test this hypothesis, we needed a measure of AS which was different from the profile approach used in previous prediction studies. Our strategy in the present investigation was to get a summary measure of *all* of the negatively toned affective remarks occurring during the interaction, irrespective of whether they were the low-frequency harsh codes or relatively benign ones (e.g., benign criticism, occasional neutral intrusiveness). Using AS in this way, one can think of a total of all of the five negative codes as a combined score, reflecting the general family emotional atmosphere or climate.

Our central hypothesis was that after three months of treatment, family management would reduce the family's combined AS score, relative to those in individual treatment, and furthermore that this reduction would help to account for the superiority of family management in reducing relapse in that condition. The primary goal of the larger study, however, was to help families learn to solve their real-life problems more constructively and to acquire a set of coping skills that would allow them to handle the stresses entailed in living with a schizophrenic family member in a better manner. Thus, a related question was whether families receiving behaviourally orientated family therapy changed over the course of treatment with respect to their use of constructive, non-emotional types of relating. The behavioural family therapy is targeted specifically to improve these coping skills; attempts to modify emotional relating styles are not the primary focus. In this particular study, we asked whether family therapy increased problem-solving skills, and if so, how this increment might increase understanding of why family affective style changes.

Method

Subjects

A total of 33 patients participated; all had a classification of schizophrenia on the Present State Examination/CATEGO criteria (Wing *et al*, 1974) and met DSM-III (American Psychiatric Association, 1980) criteria for schizophrenia. From the original sample of 36 who completed the treatment study, post-test family assessments were unavailable for two cases (one of them a relapse case), and in one case, the father did not participate in the post-test assessment. This reduced the total n for the present study to 33. All patients were between 18 and 45 years of age, resided or were in daily contact with one or both biological parents, and used English as the principal language within the home. After informed consent was obtained from family members, the patients were randomly assigned to receive either family or individual therapy.

A more detailed description of the socio-demographic characteristics of the sample is available elsewhere (Falloon *et al*, 1982). Briefly, the sample contained twice as many men as women, and a substantial number of blacks ($n=13$), Hispanics ($n=6$), and Asians ($n=2$). For both groups, the mean age of onset of disease was 22 years, and mean number of psychiatric admission was three. The average age of the patients at time of entry into the study was 25.6 years. Socio-economic status was middle to lower-middle class. Approximately half of the families were single-parent households; the others were dual-parent.

Treatment protocols

Family management was compared with individual-based management, as currently practised in many outpatient after-care programmes for schizophrenics. Patients were not entered into the study until they had attained a stable baseline of symptoms and social functioning, and were not showing any further benefit from neuroleptic medication. Random assignment was carried out once each patient had become clinically stabilised after an acute episode of schizophrenia, as defined by the PSE (four to six weeks after discharge). In both conditions, patients were seen weekly during the first three months, then every other week for the next six months. All patients were carefully maintained on optimal dosages of neuroleptic medication throughout the duration of the study. The family therapy approach used in this study has been described in detail elsewhere (Falloon *et al,* 1984). For the purpose of the present study, the two treatment conditions will be described briefly.

The family management intervention was a home-based, behaviourally-orientated, problem-solving approach, in which family members first received two sessions of education about the nature, course, and treatment of schizophrenia. Subsequent sessions focused on teaching the family a structured problem-solving method for solving family issues or problems. The therapy tended to be directed towards specific issues of problem-solving and communication that were functional deficits in each family, and it did not primarily focus on changing negative AS types of behaviour on the part of family members.

In contrast to the family interventions, the comparison treatment was clinic-based, individual supportive psychotherapy: patients in this group were assisted with problems of everyday living and management of their illness. Like the family treatment group, these patients received optimal maintenance pharmacotherapy, comprehensive crisis intervention, case management services, and education about the nature, course and treatment of schizophrenia.

Direct interaction procedure

During the initial pre-treatment phase (baseline), families in each group participated in two audiotaped direct interaction tasks involving the parent(s) and the patient. This procedure was then repeated after three months of treatment. These direct interactional data were used to measure affective style.

The structure of the interaction was a modification of the revealed differences technique developed by Strodtbeck (1954). Family members were asked to discuss a problem they held in common and to attempt to resolve their differences; this procedure is described in more detail by Doane *et al.* (1981). For both interactions, the family was instructed to discuss the topic, express their respective feelings and ideas about the problem, and make some attempt to resolve the issue; they were left alone for ten minutes. Verbatim transcripts of these discussions were used for the analysis of AS.

Affective style measure

A critical incident model of coding was used to measure the parental AS behaviour directed toward the patient during the interaction. A unit for analysis was defined as up to six consecutive lines of uninterrupted speech by a single speaker. The unit was ended when a second speaker either significantly interrupted the first or began a distinct reply. The following is a description of the negative codes in the AS scoring system;

1. Criticism (a) *Benign criticism.* The criticism is circumscribed, matter-of-fact, and/or directed toward specific incidents or sets of behaviours. Example: "You don't help with the housework." (b) *Personal criticism.* The criticism has one or more of the following qualities: unnecessary or overly harsh modifiers; reference to broad classes of behaviour; or reference to the person's nature or character. Example: "You have an ugly, arrogant attitude."

2. Guilt induction. Statements with guilt-inducing impact have two components: they convey that the patient is to blame or at fault for some negative event *and* that the parent has been distressed or upset by the event. Example: "You cause our family an awful lot of trouble."

3. Intrusiveness. Intrusive statements imply knowledge of the person's thoughts, feeling states, or motives when in fact there is no apparent basis for such knowledge. (a) *Critical intrusiveness.* The intrusiveness contains a harsh critical component. Example: "You enjoy being mean to others." (b) *Neutral intrusiveness.* The intrusiveness has a neutral quality and refers to the patient's emotional states, ideas, or preferences. Example: "You say you're angry at us, but I think you're really mad at yourself."

Reliability

Inter-rater reliability of the AS codes was previously established on another sample (Doane *et al,* 1981). Agreements on non-occurrence were not included in the calculations. Inter-rater reliability was computed using Cohen's (1960) Kappa, applied only to those instances in which one or both raters believed one of the codes was applicable, and was 0.78, $P<0.001$. *Intra*rater reliability was above 0.95 for all codes (Pearson r; 2-month interval). The transcripts in the present study were coded by two raters who were blind to any family characteristics and to which treatment condition the patient was in.

Affective style scores

Three AS indices were used for the analyses reported in the results section. For dual-parent families, these indices are based on the sum of both parents' codes across the two interactions. For single-parent families, the indices reflect the sum of the one parent's codes across interactions.

1. *Combined AS score*—the raw sum of all of the negative AS codes; this score reflects an estimate of the overall amount of negative emotionality being directed at the patient during the interaction.
2. *Total criticism score*—the sum of all of the benign criticism, personal criticism, critical intrusiveness, and guilt-induction codes; this score reflects that part of the combined AS score which is primarily critical in nature.
3. *Total intrusiveness score*—the sum of the statements coded as neutral intrusiveness. As such, it reflects that part of the combined AS score which is made up of intrusive or invasive (but not critical) remarks.

Problem solving style

A system for assessing the problem-solving responses of family members during the direct interaction task was developed by the senior author (JAD). In this system, called Problem Solving Style (PSS), 11 different categories of problem-solving statements are coded from typed transcripts of the interaction. Portions of this system were adapted from an instrument employed in research by Robin *et al.* (1977). The total score reflects the degree to which family members implemented techniques of solving problems taught to them in the family therapy sessions. The system was designed so that statements coded for AS were mutually exclusive from those coded for PSS. The codes included statements such as: specifying the problem, transition statements, proposing a solution, and planning implementation of a proposed solution. A summary score of the total number of parental PSS statements was calculated at both baseline and at the three-month post-therapy reassessment. Inter-rater reliability for the summary score was 0.91 (Pearson product-moment coefficient).

Relapse

The major criterion of patient outcome used was whether a clinical relapse occurred during the first nine months of treatment. Defining relapse is a difficult issue that often poses real problems in establishing meaningful criteria (Falloon *et al,* 1983). We were interested in whether changes in the general family emotional atmosphere were associated with the likelihood of clinical relapse; the measures that follow were used to form an operational definition of relapse.

Clinical exacerbation. This measure was used to estimate the severity of illness throughout the nine-month follow-up period. It was judged to have occurred if the team of three clinicians unanimously agreed that there had been a return of florid symptoms of schizophrenia that lasted for at least one week or required a major change in management (e.g. hospital admission or a substantial increase in the medication dosage). Since it was made by the team of clinicians doing the therapy, this dichotomous judgement was not blind.

Target symptom ratings (TSR) These ratings were carried out at baseline and at monthly intervals throughout the nine-month period by clinicians who were blind to the treatment condition of the patient. Two or three florid symptoms of schizophrenia in each patient (i.e. target symptoms), characteristic of that patient's acute episodes, were selected prior to entry into the study, were then rated on a seven-point scale of severity each month, and an average TSR score, calculated at monthly intervals.

Definition of relapse Information to determine whether a patient had suffered a relapse or significant exacerbation was available from several sources; the two measures outlined above were the main criteria used to define relapse. One criterion was whether the treating team of clinicans unanimously agreed that the patient had relapsed (clinical exacerbation). Eight patients in the individual group and one in the family group were judged as relapsers, using this criterion. A second criterion was whether the patient received a markedly serious elevation on his mean TSR. A cutting score of five on this scale was used to classify patients as relapsers, on the basis of these blind ratings. There was considerable overlap between the non-blind clinical judgement designation and the blind TSR method of grouping patients. Of the ten patients judged as clinical relapsers, seven also had elevations on the TSR. The total number of patients who met one or both of these criteria was ten.

In addition to the cases who met one or both of the above two criteria for relapse, four others were admitted during the nine-month period—two from the family group and two from the individual group. Hospital records indicated that only one of these patients was admitted for exacerbation of schizophrenia; two were admitted for drug overdose without psychotic symptoms, and one for transient lodging. Since we were concerned in this analysis with the relation of AS to the exacerbation of schizophrenic symptomatology, and not hospitalisation *per se,* we included in the relapse group only the case who was admitted (twice) for schizophrenic exacerbation but who was not judged a relapse or rated as elevated on the TSR. (This occurred because it was not possible to carry out TSR ratings or clinical evaluation by project staff.) This left a total of nine relapsers in the individual group and one in the family group.

Results

Since systematic sex differences were not found for any of the analyses, male and female patients were grouped together for data analysis purposes.

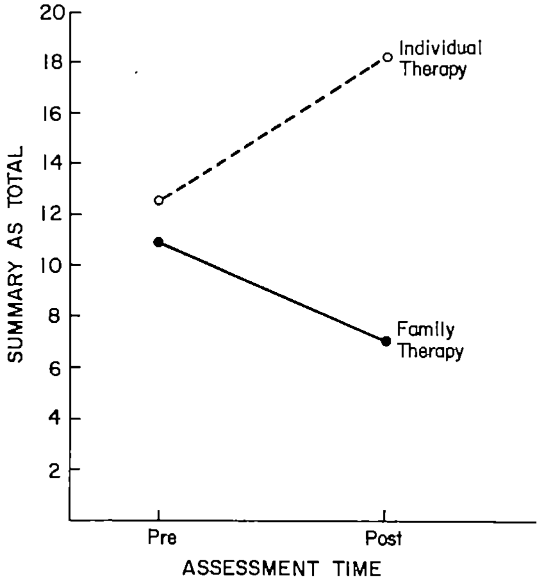


FIG. 1 Pre-post change in summary AS (Affective Style)

Impact of Treatment on Combined AS Score

The first question asked was whether there was a decrease in the combined AS score for families in the family management condition, compared to families of individually treated patients. To test this, a 2 × 2 repeated measures analysis of variance was carried out, with treatment condition and time as the independent variables and combined AS score as the repeated dependent factor. After three months of therapy, the combined AS score had markedly increased in the individual condition and decreased in the family management condition ($n=33$; d.f. = 1, $F=8.25$, $P<0.01$, for the interaction) (Figure 1). Within-group t-tests were significant for the individual condition ($n=16$, d.f. = 15, $t=2.25$, $P<0.05$, two-tailed test), indicating an increase in combined negative AS over time. For the family group, a nearly significant trend was observed ($n=17$, d.f. = 16, $t=1.78$, $P<0.10$, two-tailed test) in the direction of a decrease in combined AS. Between-group simple main effects for treatment group at the pre-test were not significant ($\bar{X}$ combined AS score for the individual group was 12.6 statements; and 10.9 for the family group.) The post-test group differences were significant, however, (18.2 statements for the individual group, and 7.0 for the family group) $n=33$, d.f. = 1, $F=13.67$, $P<0.001$).

The family management treatment was clearly superior to individual management in reducing the total number of negative emotional communications made by the parents (Figure 1). It is important that not only did the individual treatment fail to reduce AS, but over time, it increased significantly. However, the pattern of group means does not say anything about how many actual families reduced their combined AS from the pre- to post-therapy assessment. We therefore grouped the families into two categories: *increase*—those whose post-pre difference was positive; and *decrease*—those whose difference score was negative or zero. Twelve of the 17 (71%) families in the family treatment decreased their combined AS score whereas in contrast, the predominant change in the individual condition was an increase in negative AS (11 of 16 cases or 69%). Of the nine relapse cases in individual treatment, seven came from families whose combined AS increased. The one family treatment relapse was in the decrease group (Table 1).

TABLE I

Change in combined AS in individual and family therapy treatment

Treatment group	*Change in combined AS score* *Increase*	 *Decrease*
Individual	11	5
Family	5	12

Fisher's Exact Test; $P=0.04$

Impact of treatment on criticism and intrusiveness

We next investigated whether treatment might be differentially affecting two key dimensions of family affective communication: criticism and intrusiveness. British work treats criticism and over-involvement as independent dimensions in defining EE status. The codes in the affective style system can be broken down into two somewhat parallel components—criticism and non-critical intrusiveness. Perhaps treatment influences one of these dimensions more than the other. To examine this issue, two 2 × 2 repeated measures analyses of variance were carried out, with pre- to post- Total Criticism and Total Intrusiveness scores as repeated dependent factors, respectively, and treatment group and time as the independent factors in both analyses. The changes in these two variables in the two treatment groups between baseline and the three-month, post-therapy assessment are indicated in Figure 2. The AS × treatment interactions for criticism and intrusiveness were both significant in the expected direction (criticism: $n=33$, d.f. = 1, $F=5.41$, $P<0.03$; intrusiveness: $n=33$, d.f. = 1, $F=5.24$, $P<0.03$).

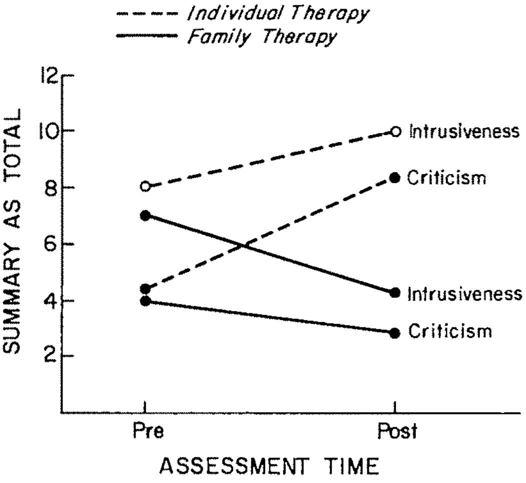


FIG. 2 Pre-post change in criticism and intrusiveness

Within-group t tests were significant for the increase in criticism observed in the individual group ($n=16$, d.f. = 15, $t=2.84$, $P=0.01$), but not for the decrease observed in the family condition. Thus, with regard to criticism, the most dramatic change occurred in the individual management group. These parents, who did not receive family treatment, dramatically increased their level of criticism towards the patient, despite the fact that their son or daughter was in weekly individual therapy throughout this three-month period. Family management apparently functioned to 'hold' or 'contain' the criticism in the parents and prevented it from escalating, rather than dramatically reducing it.

Between-group simple main effects for the treatment group at the pre-test were not significant ($\bar{X}$ Total criticism score for the individual group was 4.4 statements, and 4.0 for the family group. The post-test group differences were significant, however, (8.3 statements for the individual group, and 2.8 for the family group) $n=33$, d.f. = 1, $F=7.62$, $P<0.01$.

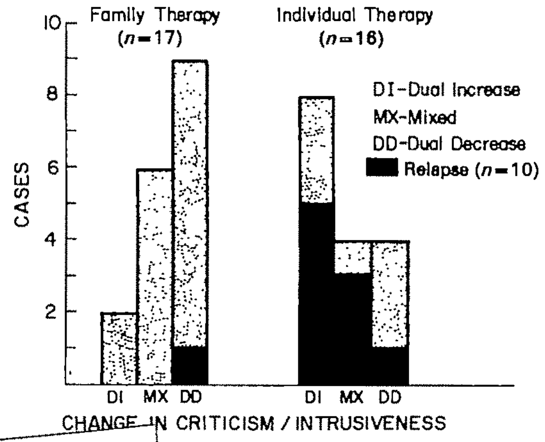
With the intrusiveness dimension, the picture is reversed. The within-group t tests for this variable were not significant for the increase in the individual group, but *were* for the *decrease* in the family management condition ($n=17$, d.f. = 16, $t=2.48$, $P<0.03$). Thus, the family intervention used in this study was less effective in reducing total criticism than it was in decreasing non-critical intrusive or invasive statements. This is not surprising, since parents in the family management group were actually encouraged to use criticism of the benign sort, and no attempt was made to reduce it.

Between-group simple main effects for the treatment group at the pre-test were not significant ($\bar{X}$ Total intrusiveness score for the individual group was 8.2 statements, and 6.9 for the family group). The post-test group differences were significant, however, (9.9 statements for the individual group, and 4.2 for the family group) $n=33$, d.f. = 1, $F=9.25$, $P<0.005$.

In sum, without family intervention, criticism rose dramatically, but did not accelerate if the family was involved in the treatment. Intrusiveness, was reduced with family treatment, but remained basically stable in individual treatment.

All but one of the relapses occurred in the individual management condition. Given the pattern of relationships (Figure 2), we next investigated how changes in one or both of these dimensions of affective climate might relate to relapse; e.g. whether families in which both criticism and intrusiveness rose had a higher relapse rate than families where both dimensions declined.

In order to pursue this hypothesis, it was necessary to divide the families in each treatment condition into three groups: (1) *dual increase* (DI), in which both criticism and intrusiveness increased from pre- to post-test; (2) *dual decrease* (DD), where both declined (or stayed the same); and (3) a *mixed* (MX), group in which one attribute increased while the other decreased or stayed the same.



ily change pattern, treatment and relapse

Figure 3 presents the frequency of each type of family change pattern by treatment group. It also indicates the number of relapses that occurred in each of these pattern-based category groups.

The modal family pattern of change for the two treatment groups differed dramatically. In the individual condition, the most common outcome after three months of treatment was a dual increase pattern i.e. parents were more critical and intrusive toward the patient (8 out of 16 cases). This pattern was observed in only two of the family-treated cases. A mirror-image is observed when one examines the modal change pattern for cases in the family management condition, where a reduction in both criticism and intrusiveness was predominant (9 out of 17 cases). Conversely, only four of the 16 individually treated families had this pattern. The mixed pattern, in which one dimension increases while the other decreases, was equally common in both treatment conditions. Thus, there is a clear trend for a reduction in one or both forms of the negative AS dimensions in the family treatment condition (15 out of 17 cases, 88%).

The relapse rate among these sub-groups differs widely (Figure 3). Examining the probability of relapse within the two modal change patterns for the individual and family-treated cases, the rate is 63% for those in the individual management dual increase group, whereas in sharp contrast, the relapse rate for the family management dual decrease families is only 11%.

Three out of the four mixed cases in individual treatment relapsed. Thus, for patients in individual treatment, risk of relapse was relatively high unless *both* dimensions of AS decreased: 67% of cases in the dual increase and mixed groups relapsed versus 25% of those in the dual decrease group. There were eight cases in the family therapy condition with the dual increase pattern ($n=2$) or the mixed pattern ($n=6$) who did not relapse. It is important to remember that this reassessment of the families occurred after only three months of family therapy, and it is possible that with sustained therapeutic contacts over the subsequent six months, changes in the affective climate of these families did occur.

The above results support the notion that a reduction in the overall level of negative affective communication can be achieved with family therapy. This intervention also significantly reduces the risk for relapse. Exactly *why* this reduction in overall AS occurred is less clear: reducing or eliminating negative emotional interaction was not the major focus of the treatment. Rather, the primary aim of the family therapy intervention was to teach families a defined, step-by-step method of solving problems. At this point, we hypothesised that treatment-induced increments in problem-solving behaviour might help to explain the observed decreases in AS.

Changes in PSS

A measure of constructive problem-solving behaviours (PSS), derived from the interaction task, was available for the parents for both the baseline and three-month, post-test interactions. The two treatment groups did not differ with regard to PSS score at pre-test. A repeated measures analysis was used to examine the relationship between changes in PSS from pre- to post-test in the two treatment conditions. The analysis revealed an interaction between treatment group and PSS ($n=33$, d.f.$=1$, $F=6.08$, $P<0.02$). Parents in individual treatment did not change in their problem-solving behaviour from pre- to post-test (from eight to ten statements). However, for those in the family condition, a dramatic increase was observed (from 10 to 25 statements) (Figure 4). Between groups, simple main effects for treatment group at the pre-test were not significant. The post-test effects, however, were significant ($n=33$, d.f.$=1$, $F=7.75$, $P<0.01$).

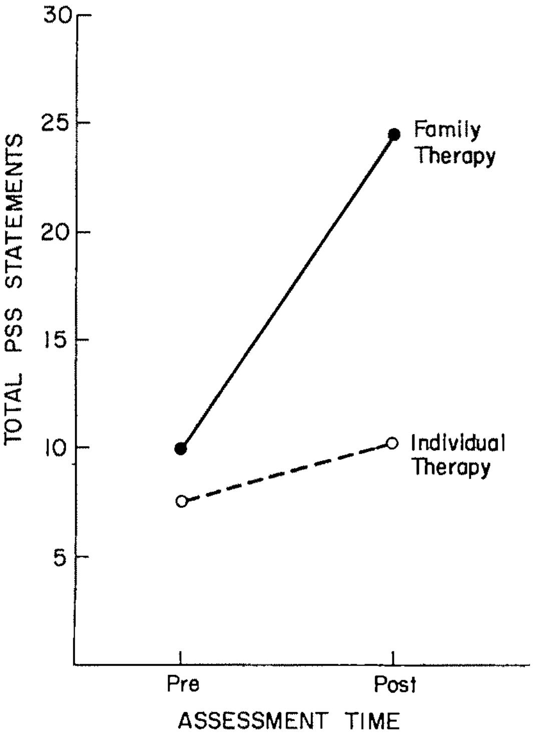


FIG. 4 Pre-post change in PSS (Problem Solving Style)

The data suggest that the families are perhaps reducing their negative affect because of a concomitant rise in the usage of non-affective types of problem-solving verbal behaviour. Since AS and PSS are mutually exclusive codes, yet both are measured from the same sample of verbal interaction, any increased in one must be accompanied by a probable decrease in the other.

Additional analyses revealed that among the individually treated group, change in affective style was a better predictor of relapse than was PSS. Since there were virtually no relapses in the family condition, the association between AS and PSS to relapse cannot be examined. Although the biggest increments in PSS occurred in families where both dimensions of AS declined, changes in PSS cannot explain the changes in AS that were observed.

Discussion

The major finding in the present study is that a significant reduction in the overall negative affective climate of the family occurred when schizophrenics were treated with family as opposed to individual management. Family therapy very dramatically reduced the likelihood of early relapse in this sample of adult schizophrenics. It also significantly increased the parents' ability to use non-emotional, constructive ways of talking to the patient during an emotionally charged discussion. Since an emotionally stressful home environment has been linked to increased probability for relapse (e.g., Vaughn & Leff, 1976a), a logical conclusion to be drawn from the present study is that reducing the level of negative affect expressed by family members helps to prevent relapse.

The findings here suggest that parents of recently discharged schizophrenics who do not receive family treatment may become more frustrated with trying to cope, as the post-hospitalisation period lengthens, and may express some of this stress by becoming even more critical or intrusive towards the patient. This finding is consistent with the widely accepted notion among clinicians that close relatives of persons in individual therapy often experience distress once treatment gets underway. When an acceleration of affect was observed in this particular sample, the probability of relapse was quite high. This finding is consistent with the earlier report on this sample, which showed that families in which the low-frequency harsh AS marker codes (such as blatant hostility and guilt-inducement) persisted, had a very high likelihood of relapse (Doane *et al*, 1985). The present findings suggest that apart from the harsh marker codes, more subtle, less blatant forms of negative relationship are also changing; when the 'emotional temperature' rises across time, the family environment continues to be a stressful environment for the relapse-prone patient, which may in some cases exceed his capabilities for coping, and result in a return of psychotic symtomatology.

The results also demonstrate that family therapy can lower the 'emotional temperature' of the home environment, and suggest that this may be due to the fact that specific, constructive ways of handling stress-producing problems were learned by the family. If so, it would follow that although negative remarks do not necessarily disappear from heated family discussions, they become less frequently the primary or exclusive modality for expression of tension or dissatisfaction about some problem with the patient. The net effect of such a change in interactive style could, theoretically at least, cause the family (including the patient) to experience the home environment as a less unpredictable, affect-laden, or emotionally stressful arena to deal with the day-to-day stresses of life.

In this study, the patient living in a home where both criticism towards him *and* intrusions into his inner life increases, appears to be at a clear disadvantage. However, a comparable disadvantage exists for the individually-treated patient whose parent(s) increases only one kind of emotional negativity. This would suggest that the importance of successful family treatment lies in the extent to which it is able effectively to reduce the overall emotional temperature of the family environment and, concomitantly to provide the family with alternative ways of coping with patient-related problems. Individually-treated patients whose families accomplished a reduction in both AS dimensions without systematic family intervention were far less likely to relapse. These findings are consistent with the notion that the overall family affective environment is an important intervening variable in the course of the illness.

The question of which discrete components of family treatment cause or interact with other variables to result in a reduction in overall affect cannot be answered in this study. The data are suggestive, however, that at least in this particular study, improved ability to cope with family stresses and problems (i.e. increased PSS) operates as a substitute for emotional ventilation. It would appear that when decreased AS was achieved, the family was better able to focus on constructive problem-solving strategies and perhaps attitudes. Thus, the data suggest a marked reciprocity between uncontrolled, negative affective expression focused upon the patient and a more controlled, cognitive form of behaviour focused on common family problems.

The design of the study did not allow us to manipulate AS and PSS independently, and therefore we cannot speak to the sequential linkage between these two dimensions of family behaviour. Unfortunately, studies of this sort are difficult to do, since in real life the affective and cognitive dimensions of interpersonal exchanges are inextricably tied together. However, efforts are needed to disentangle the discrete components of family interventions, in order to understand better how the family emotional atmosphere affects the course of illness, and what contribution to prevention of relapse is made by the modification of the affective climate by a family thèrapy approach.

The findings, if replicated, have important implications for the treatment of schizophrenia, but this study had some limitations. The cases did not constitute a typical sample of schizophrenics: all of them were living at home with at least one biological parent. The sample was small, predominantly high-EE, and all agreed to participate in a two-year treatment programme. These factors should be kept in mind, when attempting to generalise the findings. Also, this study compared a home-based, family management program with clinic-based, individual treatment, so that the setting in which treatment took place is confounded with the type of treatment delivered. Because of this aspect of the design, it is not possible to assess whether home visits *per se* influenced the outcome of patients or the changes observed in the affective climate of the family.

Acknowledgements

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*Jeri A. Doane, PhD *Assistant Professor of Psychiatry (Psychology), Yale University School of Medicine, and Yale Psychiatric Institute, P.O. Box 12A, Yale Station, New Haven, Connecticut, 06520, USA.*

Michael J. Goldstein PhD *Professor of Psychology, University of California, Los Angeles, California, USA.*

David J. Miklowitz, MA *Research Associate, Department of Psychology, University of California, Los Angeles, California, USA.*

Ian R. H. Falloon, MD MRC Psych *Associate Professor of Psychiatry, University of Southern California School of Medicine, Los Angeles, California. Consultant Physician (Mental Health), Buckingham Hospital, Buckingham, Bucks.*

*Correspondence

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Early Life Events and Affective Disorder Revisited

C. FARAVELLI, E. SACCHETTI, A. AMBONETTI, G. CONTE, S. PALLANTI and A. VITA

The incidence of traumatic events during the first ten years of life was investigated in two groups of patients suffering from major affective disorder, as well as in mixed psychiatric patients and in healthy subjects. While there were no significant differences between the two groups of affective patients or between the two control groups, the incidence of subjects who underwent such trauma was significantly higher in depressives, compared with controls. These differences are small and are further reduced if events secondary to psychiatric disturbances of family members are excluded.

In 1912, Abraham wrote that childhood trauma predisposed the individual to invest later loss events with excessive meaning, and thus played a key role in the pathogenesis of depressive disorders. Following Freud's agreement with this assumption (1917), it became an integral part not only of psychoanalytical theories but also of other approaches (e.g. Seligman 1973). This theoretical model has been tested empirically by investigating whether depressives underwent more traumatic events during childhood and/or adolescence than non-depressives, but the results are contradictory and difficult to interpret. In two recent reviews, Lloyd (1980) and Paykel (1982) observed that scarcely more than half the studies found an excess of traumatic childhood events in depressives as compared to controls. The discrepancies between these results can be attributed to several factors. Firstly, the diagnostic criteria used to select subjects were very restrictive in some cases (e.g. manic-depressive psychosis—Oltman *et al*, 1952; Pitts *et al*, 1965), while other authors adopted a broader concept of depression (e.g. Brown *et al*, 1977). Secondly, the type of event investigated and the period on which the inquiry was focussed (from the first eight years of life—Caplan & Douglas, 1969—to the first 19 years—Oltman *et al*, 1952) have been equally varied. Thirdly, differences are also found in the selection of the control group: census data (Dennehy 1966; Hopkinson & Reed 1966; Brown 1961), the general population (Brown *et al*, 1977; Oltman *et al*, 1952) medical patients (Brown 1961; Forrest *et al*, 1965; Munro & Griffiths 1969; Roy 1978; Pitts *et al*, 1965), and mixed psychiatric patients (Hill & Price 1967; Pfohl *et al*, 1983) have all been used.

The subject is further complicated by methodological difficulties, which have not always been sufficiently taken into account. On the one hand, a meticulous matching for age, social class, and age of parents would seem to be indispensable for studies of this type, since such factors influence the probability of occurrence of loss events (Granville-Grossman 1968). On the other hand, even positive results lend themselves to differing interpretations. For example, the possibility of a common genetic factor influences both the probability of the event (in relation to a psychiatric disturbance suffered by a member of the family) and the risk of an affective disorder.

Another methodological question merits consideration. Psychological models for depression are concerned with the quality of the events, rather than with their crude objectivity, so that the problem of the individual meaning of the event is central to this kind of inquiry, as it is in research into recent life events. As in the latter case, therefore, the investigation of objective childhood traumata presupposes the hypothesis that, even considering inter-individual difference, the meaning attached to the same event in similar circumstances is to some extent analogous for different individuals. The individual meaning attached to any event would therefore consist of a personal, subjective portion, plus another portion which is shared by others, as which may be referred to as 'group meaning'. In sufficiently large samples of people experiencing the same event, therefore, inter-individual differences will cancel each other out, and the resulting meaning will be the measure of that part of the single meaning which is common to all. If the group meaning represents a sufficiently ample portion of the various individual meanings, then "the aggregate results for a number of individuals will approximate the truth" (Brown & Harris 1978). As a consequence of these arguments, the results of the studies of early life events give empirical support to the theoretical psychological model only in the case of positive results. Negative results, on the contrary, could be due either to the invalidity of the theoretical model or to the fact that the collective meaning of the events does not account sufficiently for the individual meanings. In other words, the loss of the personal significance would not be compensated by the group meaning. In the latter case the explanation for the lack of meaningful results for the model being tested would be the unsuitability of the research procedure.

These difficulties notwithstanding, a further study of the frequency of childhood traumata seemed worthwhile in two separate groups of patients suffering from affective disorders, with an attempt to control the methodological difficulties as far as possible. The sample was chosen on the basis of standardised diagnostic criteria (according to the DSM III criteria) (APA, 1980), and an attempt was made to evaluate separately possible genetic factors in determining childhood events. The decision to investigate only those events which occurred in childhood was based on the fact that psychoanalytical theory regards early experiences as particularly formative and ascribes a much higher value to them than to later experiences. The first ten years of life were chosen for the present study because the tenth year represents a very definite marker, being the end (in Italy) of the first stage of compulsory education.

Our aim was to investigate the actual incidence of the events and not perception of them. Recall of the events could be influenced by the patient's depressive condition (Blatt *et al*, 1979) and by the effect on retrospective evocation of factors including the subject's personality and subsequent personal history (Yarrow *et al*, 1970; Wolkind & Zajicek-Coleman 1983). Indeed, subjects with emotional pathology might search for the causes of their problems in their past, attributing a more negative value to the events than they in fact warrant. Such systematic distortion on the part of the patient could lead to a vicious circle, in which what is believed to be the cause is in fact the effect of the association between events and pathology. Therefore, to eliminate the influence exerted by the affective state, the patients were interviewed at the end of treatment, when most of them were in a symptom-free state, and to ensure the validity of the recall, we chose not to use self-rating instruments. Furthermore, a preliminary test of agreement between the material produced by the subject and by an assessor with access to the same information was carried out, and those events which failed to achieve satisfactory agreement were excluded.

Method

In a structured interview, the incidence of the following events during the first ten years of the subject's life was investigated: death of one or both parents; separations from parents; parents' illnesses; their attitudes to child-rearing; the presence of other people in the family group; death or illness of grandparents; changes of residence; presence, age-difference, and quality of relationships with siblings; childhood illnesses; quality of relationship between parents. The subject's answers were recorded, and the circumstances in which the event took place and its causes fully investigated. The subject's age at the time of each event was recorded.

This procedure was followed with 63 depressed patients and 25 healthy controls as well as (separately) with another person who had access to the same information, usually a close relative. In the latter case, it was made clear that the account of the events concerned the subject on whom the investigation was focussed and not the relative who was actually doing the recalling.

The records, with probands and relatives, patients and controls randomly mixed, were examined by research staff not involved in the interviews. The division of the accounts into 'event' or 'non-event' was made on the basis of pre-established cut-off points, illustrated by examples. On the basis of the accounts, agreement between probands and relatives was generally high (kappa values from 0.74 to 1), with three exceptions: the events 'inadequacy of parental rearing', 'severe illness of the child', and 'difficulties in relationships with siblings' showed kappa values <0.50, and were therefore discarded for the continuation of the study. In these cases, probands and relatives gave descriptions which were either inconsistent or too vague and imprecise to allow a judgement to be made on the basis of verifiable facts. Other events (e.g. death of a sibling) were very rare, and were therefore grouped in a category of 'other events'. Yet other events, such as birth of a sibling, moving house, or death of grandparents seemed of little importance, since no trend emerged which distinguished patients from controls.

For the continuation of the study, only the following events in the subject's first ten years of life were taken into account: death of a parent, continuous separation (6 months) from one or both parents, and serious conflict between parents (divorce, or legal or *de facto* separation). When the consequences of an event appear in another event (e.g. separation from a parent consequent upon divorce), only the original event was taken into account: in practice, this means that the events 'separation from parents' should read 'separation for reasons other than death of parent or divorce'. As before, information about these events was collected by means of a structured interview with detailed investigation of the circumstances.

Subjects

Four separate groups were examined. The first (AF) was made up of 100 depressed patients, admitted consecutively to the Psychiatric Department, University of Florence and consecutively selected for psychopharmacological research. The criteria for inclusion were: (1) diagnosis of Major Depressive Episode according to DSM III; (2) absence of previous or concurrent non-affective psychiatric disorders; (3) initial score of at least 18 on the Hamilton Scale.

The second group (AM) was composed of 118 outpatients of the Lithium Clinic of the University of Milan's Clinical Psychiatry Institute. The criteria for initial inclusion were a diagnosis of Primary Affective Disorder according to the St. Louis Criteria (Feighner *et al*, 1972) and a Hamilton score of more than 18 at the time of admission to the Clinic. Retrospectively, all the patients also satisfied the criteria of the first group.

The two groups of affective patients (AF and AM) were homogeneous for initial symptomatology, and course and polarity of illness, but in comparison with the Florentine patients, the Milanese group revealed a slightly lower incidence of males and a lower proportion of cases in the older age-groups. The latter difference was due to the fact that in some cases, age excluded the possibility of lithium treatment.

Two comparison groups were used. The first (HC) was made up of 100 healthy subjects, selected from the employees of Florence University Hospital and their relatives, who volunteered to take part in the study. Since the hospital has over 3,000 employees, whose qualifications and social class are extremely varied (doctors, nurses, administrative and clerical staff, manual workers, students) and the controls were drawn not only from the hospital employees but also from their families, these people are likely include all the social levels found in society as a whole.

The selection of interviewees was made randomly within the matching categories. These took account of: (1) age (matched against the two groups of affective patients pooled); (2) social class; (3) sex. Social class was divided into five categories on the basis of occupation, father's occupation, educational level, and housing (number of rooms per inhabitant); since the last piece of information was not available for the AM, matching was against the AF only. However, since occupation and educational level of the AM corresponded to those of AF, it is reasonable to suppose that the groups were homogeneous as regards social class.

The fourth group, 100 control cases, (MP), was made up of mixed psychiatric patients, excluding affective disorders, of the Florence Psychiatric Clinic, chosen on the basis of the same matching variables. The distribution of the four groups with regard to matching criteria is illustrated in Table I. The subjects were predominantly female (approximately 3:2), aged between 40 and 60, and lower middle or working class: this reflects the normal recruitment of patients to the university hospitals.

Although they were not selected as matching parameters, parental age at subject's birth and educational level were found to be evenly distributed in all four groups.

Results

Table II shows the incidence of the events considered in each of the four groups. The two groups of affective

TABLE I

Characteristics of the sample (Values expressed as percentage of the number of cases)

		Affective patients Florence (AF)	*Affective patients Milan (AM)*	*AF+AM*	*Mixed psychiatric controls*	*Healthy controls*
Number		100	118	218	100	100
Sex	% Males	42	34	38	41	39
	% Females	58	66	62	59	61
Age	18–30	4	9.3	6.9	8	7
	31–40	6	23.8	15.6	15	16
	41–50	26	21.2	23.4	27	24
	51–60	32	33.9	33	31	32
	61–70	21	9.9	15.2	14	15
	71–77	11	1.7	6	5	6
Social class	I–II	11			8	9
	III	35			37	38
	IV	52			52	52
	V	2			3	1
Unipolars		75	76.3			
Bipolars		25	23.7			
Melancholics		62	61			
Non-melancholics		38	39			

TABLE II

Percentage occurrence of life events during the first ten years of life

	Affectives Florence (AF):	*Affectives Milan (AM)*	*Mixed psych. (MP)*	*Healthy controls (HC)*	χ^2 *(df = 3)*	*AF + AM vs. MP + HC* (df = 1)	*(1) AF vs. AM* (df = 1)	*MP vs. HC* (df = 1)
(Number)	(100)	(118)	(100)	(100)				
Death of mother	3	4.2	7	4	1.13			
Death of father	9	6	7	6	.98			
Death of either parent	12	9.3	12	9	.89			
Separation from mother (2)	11	11	7	10	1.25			
Separation from father (2)	15	22	7	10	11.89**	9.27**	1.75	0.58
Divorce	19	14.4	12	8	5.49	3.81	.83	.89
Other	4	4	2	0	4.78	3.98*	—	—
Any event	42	42.5	33	25	9.30*	7.90**	0	1.55

(1) Partition of χ^2 according to Kimball (1954)

(2) For reasons other than divorce

** = $P<0.01$ * = $P<0.05$

patients (AF and AM) show a large degree of homogeneity as regards early events. The two control groups (healthy and mixed psychiatric) show a rate comparable to that of the depressed patients for bereavement caused by death of parents, and for separation from the mother, but have a lower rate of separation from the father. Chi square is significant at the 0.01 level, almost entirely due to the comparison of affective patients (AF + AM) vs controls (normals and psychiatric combined). Separation of parents is slightly more frequent in the case of depressed patients than in that of healthy controls, but the difference fails to attain significance. The 5% confidence level is also attained on the item 'other events' (made up of the events 'death of sib' and very severe illness of the child) as far as the comparison AF + AM vs the two comparison groups combined is concerned. ($\chi^2 = 3.98$, df = 1).

If the occurrence of any of the events considered is examined, the four groups reveal significant distributive differences. In fact, 42% of the affective patients underwent at least one of the events considered during the first ten years of life, as compared with 25% of the healthy controls and 33% of the non-affective psychiatric patients. If the affective disorder groups are combined and compared with the pooled comparison groups, the difference in childhood experience of the traumata is significant at the 0.05 level.

The fact that a higher incidence of early events is found in the depressed patients could be related to a higher level of psychiatric pathology in the family circle. Since the interview used to collect data regarding life events investigated not only the presence of the events but also the circumstances in which they occurred and their possible causes, we tried to single out those events which might possibly have been the consequence of behavioural disorders with a psychiatric origin on the part of a member of the family. While there were no cases of parental suicide during the first ten years of the child's life, in a few cases it was discovered that separation from one of the parents was connected to psychiatric disorder (e.g. admission to a psychiatric hospital). In other cases, the separation of the subject's parents was clearly due to a psychiatric disorder (usually alcoholism or sociopathy, suffered by one or the other). We therefore calculated the incidence of early events once again, excluding these people (Table III), and the differences between depressives and controls then became much less marked. However, in two cases significant differences in the incidence rates remained: separation from the father for more than six months consecutively; and in the case of AF + AM vs. HC + MP controls only, the number of subjects who had undergone at least one event.

The incidence of childhood loss events in both depressives and controls was fairly stable throughout the different social classes, AF having experienced an approximately 15–20% excess of events in each category, as compared to HC. Thus, social class did not have any particular effect on the relationship between childhood traumata and adult depression.

The most frequent event was separation from father, mostly caused by the father's work (temporary emigration), though some were due to war service: these totalled three for AF, four for AM, two for HC, and two for

TABLE III

Percentage occurrence of life events during the first ten years of life with exclusion of events secondary to psychiatric disturbances in the family

	Affectives Florence (AF)	*Affectives Milan (AM)*	*Mixed psych. (MP)*	*Healthy controls (HC)*	χ^2 *(df=3)*	*AF+AM vs. MP+HC* (df=1)	*AF vs. AM* (df=1)	*MP vs. HC* (df=1)
(Number)	(100)	(118)	(100)	(100)				
Death of mother	3	4.2	7	4	1.13			
Death of father	9	5.1	7	6	1.43			
Death of either parent	12	9.3	12	9	.89			
Separation from mother (1)	9	11	7	10	1.10			
Separation from father (1)	15	21.2	7	10	10.73*	8.59**	1.38	0.58
Divorce	8	11.9	10	8	1.31			
Other	3	4	2	0	—	3.18	—	—
Any event	36	39	32	25	5.22	3.90*	0.21	1.20

(1) For reasons other than divorce

** = $P<0.01$ * = $P<0.05$

MP—all in the 41–50 age-group. The exclusion of these events did not modify the results of the comparison for the event 'separation from father' ($\chi^2=11.49$, df=3, $P<0.01$). Finally, the length of the separation period was also taken into consideration: in five cases (one AF, one AM, two HC, one MP) separation from mother lasted less than one year. However, the comparison for the event 'separation from mother' failed to reach statistical significance both in the case of separations of more than one year and in that of permanent separations, whereas all but one of the separations from father exceeded one year.

Comparisons between affective patients did not reveal noteworthy differences. The incidence of traumatic childhood events did not differ when patients were divided on the basis of polarity (unipolar vs. bipolar), symptomatological pattern (melancholic vs. non-melancholic—DSM III criteria—) or sex.

In the same way, the age at which the events took place (the first and second five years of life were considered separately) did not reveal significant differences.

Discussion

The two samples of affective patients were selected according to rather restrictive criteria, considering not only the symptoms (Major Affective Disorder), but also their severity (Hamilton score$>$18). The subjects had initially been selected for research of a clinical-psychopharmacological nature, so that the composition of the sample (25% bipolars, 2/3 endogenous) is closer to that which is normally found in research into biological psychiatry than to that of most recent studies of life events. Any comparisons must therefore be made with caution.

Tennant *et al*, (1981) contend that an early loss influences in different ways the probability of the development of symptoms (being a 'case') and the probability of seeking medical help (being a 'patient'). According to this argument our sample, being composed only of 'patients' and not of 'cases' would be biased, but the severity and pervasiveness of the symptoms of our sample were such that it was almost inevitable that such 'cases' should seek medical help. This is confirmed by the preliminary results of an epidemiological community survey conducted in Florence (Faravelli & Incerpi, 1985, in press), which showed that 93.3% of cases which satisfied our criteria consulted their GPs and that 87.7% of these were referred to a psychiatrist. Therefore, for our depressed subjects, 'cases' and 'patients' are closely identified.

The present study considered events of the first ten years only, whereas others have investigated a longer period, including adolescence and sometimes even later. The child's sexual development and with it the end of childhood normally occur after the tenth year, so that our investigation systematically ignored events of the early teens. This fact could have two kinds of consequences. On the one hand, it could diminish the discriminatory power of our analysis, in that the exclusion of a period could flatten out differences between groups; this might be important since, given the low incidence of some events (e.g. early death), it would be difficult for possible differences to reach significance. However, the risk of a type II error seems negligible in our findings, since there does not seem to be a trend which might permit a hypothesis of uneven distribution in any of the comparisons which do not reach significance. More important is the possibility that events occurring in the early teens might have a particularly high risk value for the development of affective disorders (Hill & Price, 1967). This fact was not considered in our original hypothesis (the empirical verification of the psychological theory), and when the study was planned an authoritative paper (Brown *et al*, 1977) had recently suggested that loss (in particular loss of mother) was related to adult depression if it occurred between the ages of 0–10, but not if it occurred 11–16.

Therefore, our data confirm the uncertainty which emerged in previous writing on the subject: a slightly greater incidence of early events seems to exist in depressives, but the increase is so small that it cannot always be measured. The relative risk for any one of the events for depressives, as compared to healthy controls, is in fact of the order of 1.6—a much lower figure than might be expected on the basis of the psychological models of the illness.

If the data are then corrected by excluding those events caused by psychiatric illnesses of members of the family, the differences become very slight indeed. Nevertheless, an excess (albeit a very small one) of events was recorded for depressives, compared to controls, even in this comparison, which in its turn could be due to other psycho-pathological conditions of the parents which our interview did not reveal. It is likely that cases connected with the major psychiatric disorders were eliminated, but certain kinds of anomalous behaviour or attitudes not associated with symptomatologically evident disorders (for example minor forms of personality disorder) were probably not revealed. This means that our analysis should be read as exploratory, and not as a real measure of the number of events which have a genetic basis, but the results seem to give weight to the objection that a substantial portion of the loss events suffered by depressives is related to the greater incidence of psychiatric disorders in their families (Paykel, 1982).

Nevertheless, the fact remains that events connected to psychiatric disorders on the part of the parents also have a purely psychological effect on the child, and this can certainly influence the development of the personality. It is therefore impossible to decide whether inter-generational correlations have a genetic or a psycho-social basis.

The only reasonable conclusions are that: (a) an increase of early separations in depressed patients does exist; (b) part of the increase (about one quarter of the excess over the comparison groups) is connected to manifest psychiatric disorders in the family; and (c) the differences are too small to support the psychological model of the illness conclusively.

It is legitimate to ask whether these results are due to the theoretical assumptions being only partly valid, and childhood experiences not having such a great influence in determining the development of affective pathology, or whether the procedure adopted to measure early events is incapable of identifying more meaningful differences. In fact, the narrowness of the differences identified by our research could be due to the simple enumeration of a certain number of events being too clumsy a tool to measure the effective impact that life events have on a child. As in research on recent life events, the problem is of how to record the individual meaning of the events; the same event can have different effects on different children, and indeed on the same child in different contexts.

To avoid this kind of problem, self-rating methods, in which the individual evaluates the weight of the events of his childhood subjectively, have been suggested. (Schaefer 1959; Roe & Siegelman 1963; Becker 1964; Raskin *et al*, 1971; Parker *et al*, 1979; Perris *et al*, 1980). However, even more than in the case of the evaluation of recent life events, subjective questionnaires are open to various criticisms, the most important of which is that of the search for meaning (Brown & Harris, 1978). In fact, the element of retrospective judgement of the events could be heavily influenced by the outcome (whether or not the subject became ill), as well as by the subject's personality. Moreover, our data do not confirm Parker's (1981) observation that: "subjects' scores... correlated significantly with scores returned by family observers and judges". In fact, our preliminary test of reliability showed that even the simple recall of matters that require a certain amount of subjective judgement (e.g. quality of parental rearing) is biased to the extent that the agreement based on the reports of different informants drops below the level of acceptability. Subjective methods of evaluating early events may also be prejudiced since, while they give a measure of 'perceived childhood', they do not guarantee sufficient exploration of what actually happened.

The methodology for the study of childhood events seems to be crushed between the Scylla of objective methods' lack of sensitivity and the Charybdis of subjective methods' loss of reliability. Therefore, the interpretation of our data is not easy: we incline to the view that an excess of traumatic childhood events does exist in affective patients, but this is greatly reduced by the inability of the method adopted to detect such differences.

Another factor which might help explain the smallness of the difference between depressed patients and controls is the possibly heterogeneous nature of the affective phenomenon. Forms with differing aetiologies might fall into the same symptomatological pattern, and various factors, interacting variously among themselves and operating on different levels, very probably contribute to the origin of the illness. If this is the case, the investigation of only one parameter at a time can give rise only to partial differences, which are capable of explaining only a small part of the phenomenon's variability. This hypothesis is supported by the fact that none of the numerous parameters (biological, psychological, or sociological) which have so far been reported as distinguishing depressives from controls seems sufficiently specific to support theoretical models based on a single factor.

In other words, if depressive behaviour "must be understood as occurring at several levels simultaneously, rather than having a one-to-one, direct relationship with a single event" (Akiskal & McKinney, 1971), it will be necessary to investigate several factors on different levels to obtain a sufficiently comprehensive explanation of the pathological phenomenon. If so, even small differences, such as those we found, can suggest not so much the validity or otherwise of the psychological model as the necessity for its integration into more articulated theoretical models.

Conclusion

These results are capable of bearing three different interpretations: (1) the initial hypothesis, as derived from the psychological-psychoanalytical model of depression, is only partially valid; an early trauma, although an important factor, would not be as crucial to the development of affective illness as the theory suggests; (2) the method used to quantify early events is too clumsy to capture the emotional impact of these events on the child; the exploration of the few events which can be reliably ascertained by means of retrospective investigation is too restricted to be able to capture the real psychological implications. Furthermore, the simple listing of the events involves an excessive loss of their individual meaning, insufficiently compensated for by the fact that, once the context in which the events took place is known, they can be understood and evaluated by other people, thus acquiring a portion of group meaning. The loss of individual meaning would not be sufficiently compensated for by the group meaning of the events; (3) other factors, apart from those considered by the psychological model, play an important role in the aetiopathogenesis of these disorders. The differences in early events would be small, because other variables which were not taken into account modulate the development of the depressive phenomenon. This interpretation can be considered a variation of the first one, but seems to be particularly relevant, since it is supported by other data. Genetic research, research into biogenic amines, that on psycho-endocrinology, and that on receptors have revealed that certain biological factors have considerable influence on the genesis of affective disorders. However, such factors are not taken into consideration by the psycho-sociological models of the illness, just as conversely, psycho-sociological elements are not taken into account by the biological models.

We believe that the results of the present study indicate that childhood traumata play a part in the genesis of affective illnesses—a part which must be taken into consideration if we are to reach an explanation of this illness which is more than partial. On the other hand other elements, which generally have no place in the structure of psychological theories must equally be taken into account.

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*C. Faravelli, MD, *Senior Researcher.*

A. Ambonetti, MD, *Junior Doctor.*

S. Pallanti, MD, *Junior Doctor.*

Institute of Nervous and Mental Diseases, Department of Clinical Psychiatry, University of Florence, 50134 Florence, Italy.

E. Sacchetti, MD, *Associate Professor.*

G. Conte, MD, *Junior Doctor.*

A. Vita, MD, *Junior Doctor.*

Institute of Clinical Psychiatry, University of Milan, 20100 Milan, Italy.

*Correspondence

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The Evaluation of Illness Behaviour and Exaggeration of Disability

J. R. CLAYER, C. L. BOOKLESS-PRATZ and M. W. ROSS

The evaluation of illness behaviour can be complicated by subjective influences in either the patient or the clinician; these often arise in the evaluation of persons seeking compensation for injuries in which the symptoms are apparently exaggerated. The present study attempts to assess the usefulness of the CE Scale in determining the degree of conscious exaggeration by compensation claimants. Comparisons were made between psychiatrists' clinical evaluations of claimants and the scores obtained on this scale. The relationship between these two measures was found to be significant at the 1% level and specificity and sensitivity for less than 25% exaggeration on psychiatrists rating with a CE Scale cut-off of 11.69% and 100% respectively: for less than 34% exaggeration, they were 88% and 83%.

Compensation neurosis has always been a vexatious issue. Despite the large cost that this condition imposes upon the community, and despite the heavy involvement of the medical world, little is known about the condition. In reaching that conclusion in his comprehensive review of the literature on compensation neurosis, Weighill (1983) emphasised the need for research: despite the difficulties involved in the evaluation of such cases, no studies using standardised questionnaires have been carried out. Since then, Clayer *et al* (1984) have developed a scale from Pilowsky & Spence's (1975, 1983) Illness Behaviour Questionnaire, the CE Scale, which discriminates between conscious exaggerators, neurotics and normal respondents.

The evaluation of any illness behaviour, normal or abnormal, is never simple. When it is complicated by subjective experiences, either on the part of the patient or the doctor, the problem is made even more difficult. For example, in a ten-year follow-up of 40 male patients who had been diagnosed as 'hysteric' (36 conversion reaction disorders and four dissociative reactions), Watson & Buranen (1979) found that in 25% of cases, the conversion reaction diagnoses represented misdiagnosed physical disease. Their findings supported earlier, and similar work by Slater & Glithero (1965) and by Whitlock (1967). Watson & Buranen found that the conditions most often mislabelled as 'hysteric', were those involving degenerative conditions of skeletal, muscular and connective tissue. Two of those three are conditions in which it is extremely difficult to find positive physical evidence of injury.

The importance of accurate and early assessment of such symptoms, in cases of accident neurosis presenting for litigation, has been demonstrated by Tarsh & Royston (1985) in their follow-up study of 35 such cases.

Miller (1961) spoke strongly of the doctors' inability to distinguish between accident neurosis and malingering in their reporting of these cases in court. "Whether such exaggeration is conscious or unconscious is a question often debated between lawyers and psychiatrists in court. To many psychiatrists it presents no problems, and they authenticate the complainant's unawareness of motivation with a confidence that seems impressive—until one reflects that differentiation between conscious and unconscious purpose is quite insusceptible to any form of scientific inquiry, and that it depends on nothing more infallible than one man's assessment of what is probably going on in another man's mind".

These views are supported by the work of Simon & Zusman (1983), who systematically analysed the psychiatric reports provided by both sides in a major psychic injury lawsuit following the Buffalo Creek disaster in the U.S. They found that the psychiatrists for the two sides came to the same diagnosis in only 12% of cases; psychiatrists for the plaintiffs approached examinations psychodynamically, while defendents' psychiatrists approached them descriptively. In their view, part of this bias pre-existed in the psychiatrists prior to their involvement in the case, and the remainder appeared once their identification with a particular side had taken place. Clearly, there is a need for more objective and standardised measures of conscious exaggeration of symptoms associated with litigation.

The present paper describes a preliminary clinical testing of the measure of conscious exaggeration (the CE Scale) described by Clayer *et al* (1984).

Method

Two psychiatrists were selected on the basis of their objectivity, (as reported by insurance companies and lawyers); both were asked to assess the degree of conscious exaggeration being used by ten consecutive persons referred to them for evaluation of physical symptoms following injury, believed by the persons' legal advisers to be at least partly of psychological origin. Referrals included those from the legal advisers of both the plaintiff and the defendant.

An assessment was made by the psychiatrists of ten patients each, immediately following the interview, on a scale of 0–100, where 0 represented no conscious exaggeration and 100 represented complete fabrication of symptoms and signs. At the end of the psychiatric interview, the subject completed the Illness Behaviour Questionnaire (IBQ) (Pilowsky & Spence, 1983), under the supervision of the research officer. When 20 reports had been completed, the Spearman correlation coefficient between the psychiatrists' evaluation and the CE Scale was calculated, and the two sets of scores examined graphically.

Three subjects refused to complete the IBQ, and these were replaced by the next referred persons. Of the 20 subjects, eight were born in Italy, seven in Australia, four in Yugoslavia, and one in the United Kingdom. Greek-speaking subjects were excluded because of the unavailability of a Greek translation of the IBQ, at the time. The IBQ had been translated into all other appropriate languages and, where necessary, the translated form was used in the presence of a translator.

The age range was 22–56 years, mean 41.8; however, the CE Scale has been shown to be unrelated to age; 11 subjects were male, nine female. The nature of their injuries was that six subjects complained of injuries involving predominantly their back, four their shoulder, three their neck, two their leg, four their hand/wrist, and one their arm. At time of examination, for six subjects the condition had been present for one year only, for three subjects two years, for five subjects three years, two subjects four years, and for four subjects five years or more.

Results

The scores arrived at by the psychiatrists and by means of the CE Scale, are represented graphically in Fig. 1.

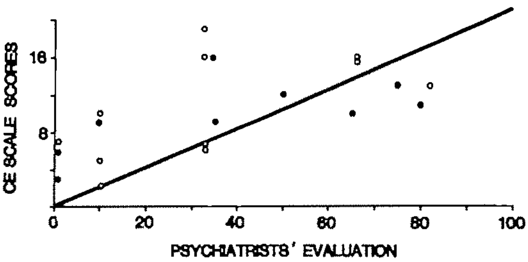

FIG. 1. Conscious exaggeration by CE scale scores and psychiatrists' evaluation.
(Psychiatrist "A" = ○); (Psychiatrist "B" = ●)

The line representing perfect correlation is drawn between those figures. For the majority of the psychiatrists' evaluative scores there is some approximation with the CE Scale, and the overall correlation coefficient between psychiatrists' scores and CE scores is 0.64, (P<01). Individually, psychiatrist A achieved a correlation coefficient of 0.57 with the CE Scale, (P<0.05), and psychiatrist B a correlation coefficient of 0.71, (P<0.05).

For both psychiatrists, four cases are clearly disparate with the CE Scale. In all but one of these cases this represents an undervaluation by the psychiatrist in terms of the CE Scale. Sensitivity and specificity of the CE Scale were calculated using two assessments of percentage of conscious exaggeration: less than 20% and less than 34%, and with a cut-off on the CE Scale of less than 11. Sensitivities were respectively 69% and 88%, specificities respectively 100% and 83%.

Discussion

The two psychiatrists involved in this study obtained an overall correlation coefficient with the CE Scale scores of 0.64. This statistically significant result suggests that whatever the psychiatrists were evaluating was related to the score of the CE Scale. It is clear from the graphic representation of these scores that the correlation would have been much higher if it were not for four cases with each psychiatrist in which their evaluation of conscious exaggeration was considerably disparate from that obtained by means of the CE Scale.

One interpretation of these discrepancies is that the CE Scale provides a consistent measure of conscious exaggeration and that psychiatrists are prone to be inaccurate in about 40% of such evaluations, assuming the CE Scale to be an accurate measure. It is interesting to note that in seven of the eight cases, in which the scores diverge markedly, the psychiatrists, in terms of the CE Scale, have underestimated the degree of conscious exaggeration.

The results can also be interpreted as showing that the CE Scale is not always valid when measured against the criteria of psychiatrists' evaluation. If so, this does not, of course, render the scale useless; it cannot be an infallible indicator of conscious exaggeration. It may possibly be of value if it is used as an additional measure, to be considered in the light of all other information.

Despite the presumed objectivity of the two psychiatrists involved in the study, subjective factors clearly remained. One such factor was the difficulty in identifying and evaluating conscious exaggeration in a person who did have either clearly evident physical damage or clear-cut neurotic features. Conversely, persons with no clear-cut neurosis or physical damage were much more likely to be considered to be exaggerating consciously. However, information from insurance companies suggests that both groups are equally capable of conscious exaggeration.

Sensitivities and specificities (true positives and true negatives) must be weighed up considering the contingencies of each. We believe that it is preferable to misclassify some positives as negatives rather than to misclassify negatives as positives on the CE Scale, and have thus opted for high specificities. From Figure 1, it can be seen that there were no cases assessed by the two psychiatrists above 10% and below 33% exaggeration of symptoms, and hence the arbitrary 20% cut-off was chosen. Using a CE score of 11, no individuals were classified as conscious exaggerators who were assessed by the psychiatrists as non-exaggerators, but 30% were misclassified as being non-exaggerators on their CE scores when, in fact, they were assessed as being exaggerators. We would emphasise, however, the small sample and the preliminary nature of this work.

One case history from the 20 included in this study, although anecdotal in quality, gives some hope that the scale can be of assistance in the evaluation of conscious exaggeration. The subject was a 22-year old male, born in Italy and brought to Australia by his parents when one year of age; he was a qualified tradesman, who injured his back while involved in building construction work. He attempted to return to work but found this too painful, and consequently consulted a number of therapists. Nine months later a consultant surgeon described him as performing well and recommended that he return to work. He also commented that three weeks later, the patient had developed a considerable limp and many more symptoms.

However, the subject then appeared to gradually improve. He obtained part-time work and resumed normal social activities, including sport. Approximately two years after his accident he was seen by three psychiatrists, one of whom was a participant in the present study. One of the other two psychiatrists examined the subject on behalf of the plaintiff, one on behalf of the defendant. All three psychiatrists commented upon the subject's 'healthy, coping personality' and his optimism about returning to full time work. He was good natured, moved easily and neither complained of, nor demonstrated, any physical disability. All three psychiatrists predicted that he would continue to cope extremely well.

The CE Scale, however, indicated a score of 10. Although not dramatically high, it does indicate a tendency to conscious exaggeration beyond that expected from clinical examinations. It was with some interest that we later learned that on appearance in court only days after the psychiatric evaluations, the subject was so disabled that a wheelchair was called for.

Unfortunately, litigants are too often dichotomised into two groups, malingerers or neurotics. The reality is that in almost every case there is some degree of both physical pathology and neurotic reaction, and in many, some degree of conscious exaggeration. Cut-off points must reflect degrees of certainty rather than absolute diagnosis.

The case of the pure malingerer is rare (Nemiah 1975). However, litigation in the majority of cases, as in this study, usually extends over a period of three years or more. Slater (1961) found that 50% of patients with conversion disorders lose their symptoms within a year of first being seen. It would be surprising if a litigant with a neurotic complaint did not consciously perpetuate the symptoms upon which his income and veracity had depended for three or more years, if those symptoms began to spontaneously remit after so long a time.

The major problem in validating a scale such as this is to find standards against which to measure it. Many avenues were explored in developing this study, but all possible criteria of conscious exaggeration such as size of settlement and continuation of attendance for treatment, proved to contain too many variables. Even clearcut evidence such as filmed activities beyond the supposed capacity of the plaintiff is inadequate because of the difficulty in identifying an adequate control group.

Nevertheless, these preliminary data do suggest that the CE Scale and the two psychiatrists involved are tapping the same underlying dimensions, with over 40% of their variance in common. While further research is needed, this pilot study is encouraging and suggests that further work is warranted on the CE Scale. It must be emphasised, however, that the present study involved only a small number of subjects and that further investigation might include evidence on the agreement between psychiatrists ratings on the CE Scale, using larger numbers of psychiatrists, comparison of demographic and clinical features of high and low scorers, and more importantly, outcome studies. At present, ratings from the CE Scale cannot be regarded as providing a basis for medical or legal decisions, but these data do suggest that it has some promise and further research is warranted.

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*J. R. Clayer, MBBS, DPM, MD, FRANZCP, *Director, Mental Health Research and Evaluation Centre, 242 Greenhill Road, Glenside, South Australia, 5064.*

C. L. Bookless-Pratz, BA, Research Officer, Mental Health Research and Evaluation Centre, 242 Greenhill Road, Glenside, South Australia, 5064.

M. W. Ross, BS(Med.), MA, Dip.Tert.Ed., PhD, ABPsS, ANZPsS, MAPsS, *Senior Demonstrator in Psychiatry, Flinders University Medical School, Bedford Park, South Australia, 5042.*

*Correspondence

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The Influence of Seizure Type and Medication on Psychiatric Symptoms in Epileptic Patients

S. W. BROWN, M. E. L. McGOWAN and E. H. REYNOLDS

The influence of type of seizure and medication on psychological disability was assessed using the Standard Psychiatric Interview in matched epileptic patients. In comparison to patients with idiopathic tonic-clonic seizures, those with temporal lobe epilepsy complained of more irritability and impaired concentration, and were rated as more depressed and slowed up. Compared to patients on phenytoin, those on carbamazepine complained of more sleep disturbance and were more likely to be taking an hypnotic.

Though it is widely recognised that several important biological and psychosocial factors contribute to the relatively high incidence of psychological disorders in epileptic subjects (Reynolds, 1981; Pond, 1981; Brown & Reynolds, 1981), there is little agreement as to the relative importance of seizure type and severity, brain damage, anticonvulsant medication, genetic factors, and psychosocial stress. Thus, an extensive but conflicting literature over the last 35 years suggests that patients with temporal lobe epilepsy are especially vulnerable to psychological disorders (Gibbs *et al*, 1948; Guerrant *et al*, 1962; Reynolds & Trimble, 1981; Koella & Trimble, 1982; Reynolds, 1983a; Trimble, 1983). Over the same period, the possible influence of anticonvulsant medication had been widely neglected, but recently, evidence has grown of a relatively more important role for this factor in the psychological disorders of epilepsy (Trimble & Reynolds, 1976; Reynolds, 1983b). Carbamazepine may have relatively less adverse effects than phenytoin in this respect (Reynolds, 1983b).

There are several reasons for the controversies in this literature (Reynolds, 1983a): studies of individual factors have usually failed to control for other influences, and there has been a tendency to study a biased sample of chronic epileptic patients who have gravitated to psychiatric clinics or hospitals.

We have therefore undertaken a study of the influence of two potentially important biological factors, viz—seizure type and anticonvulsant medication, on psychological symptoms in epilepsy. This was done in a neurological clinic, in epileptic subjects whose seizures were relatively well controlled on single drug therapy with blood level monitoring, and endeavouring to control for other factors as carefully as possible.

Subjects

Fourteen patients with uncomplicated temporal lobe epilepsy and 14 patients with idiopathic tonic-clonic seizures were chosen by one investigator (MM) from the case-notes of out-patients attending the Neurology Clinic at King's College Hospital. In all cases, seizure type was documented clinically and electroencephalographically. The temporal lobe group had complex partial seizures with or without tonic-clonic attacks, and all had shown temporal spikes on routine EEG testing at some point; in the tonic-clonic group, no focal EEG abnormality had been demonstrated. All subjects in both groups had normal CT scans. The two groups were chosen to be matched in pairs as closely as possible for sex, age, social class, seizure frequency, duration of epilepsy, and current anticonvulsant drug treatment.

In addition, 16 patients on phenytoin (DPH) alone, and 16 patients on carbamazepine (CBZ) alone were chosen. All had been on this monotherapy, without evidence of clinical toxicity, for at least six months. All had a normal recent full blood count, serum folate, and serum vitamin B12 levels. These two groups were chosen to be matched in pairs as closely as possible for sex, age, social class, type of seizure disorder, seizure frequency, and duration of epilepsy.

Details of the matching in both studies are given in Tables I and II. Some patients were included in both studies, so that the total number selected was 45, consisting of 19 males and 26 females. In the temporal/tonic-clonic study, eight of the matched pairs were female and six male. In the phenytoin/carbamazepine study, nine pairs were female and seven male.

Methods

Most subjects were interviewed when they attended the clinic for their regular appointments, but a few were requested to attend specially. All interviews were conducted during an afternoon clinic by a second investigator (SWB), who was blind to the patients' diagnosis and treatment. Subjects were told that the investigator was carrying out a survey of the general health of people in the clinic,

TABLE I

Seizure type study

a. *Mean ages of subjects (yrs)*

	(*n*)	Temporal lobe	(*n*)	Tonic-clonic	(*n*)	Total
Male	(6)	31	(6)	27	(12)	29
Female	(8)	34	(8)	27	(16)	30
Total	(14)	33	(14)	27	(28)	30

b. *Social class distribution*

		I	II	III	IV	V	Total
Males	TLE	0	1	3	2	0	6
	GM	0	1	1	3	1	6
Females	TLE	0	3	2	1	2	8
	GM	0	2	4	0	2	8
Total	TLE	0	4	5	3	2	14
	GM	0	3	5	3	3	14

c. *Duration of epilepsy*

		<3 years	>3 years	Total
Male	TLE	0	6	6
	GM	0	6	6
Female	TLE	1	7	8
	GM	0	8	8
Total	TLE	1	13	14
	GM	0	14	14

d. *Medication*

		Phenytoin	Carbamazepine	Valproate	Total
Males	TLE	3	2	1	6
	GM	3	2	1	6
Females	TLE	4	4	0	8
	GM	5	3	0	8
Total	TLE	7	6	1	14
	GM	8	5	1	14

e. *Number of seizures in last 6 months*

		None	1–6	>6	Total
Males	TLE	4	2	0	6
	GM	4	2	0	6
Females	TLE	5	2	1	8
	GM	6	2	0	8
Total	TLE	9	4	1	14
	GM	10	4	0	14

TLE = Temporal lobe epilepsy
GM = Idiopathic tonic-clonic seizures

TABLE II

Medication study

a. *Mean ages of subjects (yrs)*

	(*n*)	DPH	CBZ	Total (*n*)
Male	(7)	30	31	31 (14)
Female	(9)	29	27	28 (18)
Total	(16)	29	29	29 (32)

b. *Social class distribution*

		I	II	III	IV	V	Total
Males	DPH	0	2	3	2	0	7
	CBZ	0	2	2	2	1	7
Females	DPH	0	2	4	1	2	9
	CBZ	0	3	4	2	0	9
Total	DPH	0	4	7	3	2	16
	CBZ	0	5	6	4	1	16

c. *Duration of epilepsy*

		<3 years	>3 years	Total
Male	DPH	1	6	7
	CBZ	0	7	7
Female	DPH	1	8	9
	CBZ	3	6	9
Total	DPH	2	14	16
	CBZ	3	13	16

d. *Classification*

		Tonic clonic	Complex partial	Other*	Total
Males	DPH	3	3	1	7
	CBZ	3	4	0	7
Females	DPH	5	4	0	9
	CBZ	5	4	0	9
Total	DPH	8	7	1	16
	CBZ	8	8	0	16

e. *Number of seizures in last 6 months*

		None	1–6	>6	Total
Males	DPH	6	1	0	7
	CBZ	5	2	0	7
Females	DPH	8	1	0	9
	CBZ	5	3	1	9
Total	DPH	14	2	0	16
	CBZ	10	5	1	16

DPH = phenytoin
CBZ = carbamazepine
*simple motor

and were asked not to mention the name of their medication or to discuss their epilepsy. Blood levels of anticonvulsants were measured after the interview. For DPH, the range was from 4.6–16.0 μg/mL with a mean of 8.29 ('optimum' range 10–20 μg/mL). For CBZ, the range was from 2.4–10.7 μg/mL with a mean of 5.38 ('optimum' range 4–10 μg/mL).

Each subject was administered the Standard Psychiatric Interview (SPI), a research tool designed for use in community surveys which produces scores for common psychiatric symptoms. It is a recognised research instrument of proven validity and reliability (Goldberg *et al*, 1970), provided that the interviewer has undergone training and standardisation in the technique, as was done by SWB. When all subjects had been interviewed, the code was broken and the matched pairs were compared both for total scores and for scores of individual symptoms.

Results

For all 45 subjects, the number scoring 2 or more for each item of the questionnaire (which is taken as a cut-off score indicating 'caseness') is shown in Table III.

More than 40% of all patients complained significantly of fatigue, and more than 20% significantly of somatic symptoms, depression, anxiety, and obsessional symptoms; more than 30% were rated by the interviewer as appearing significantly depressed in the interview.

For the matched pairs in the seizure type and medication study, both total scores for each subject and individual scores for symptoms and manifest abnormalities were compared using Wilcoxon's test. Items in which the difference between the two subjects' scores was zero were disregarded, and ties for ranks were broken by assigning mean values. Tables IV and V show the results for seizure

TABLE III
Total patients scoring 2 or more per item

	N	%
Reported symptoms		
Somatic symptoms	10	22.2
Fatigue	19	42.2
Sleep disturbance	8	17.8
Hypnotics	4	8.9
Irritability	6	13.3
Lack of concentration	6	13.3
Depression	12	26.7
Anxiety	10	22.2
Phobias	5	11.1
Obsession	10	22.2
Depersonalisation	4	8.9
Manifest abnormalities		
Slow	5	11.1
Depressed	14	31.1
Anxious	5	11.1
Flattened	2	4.4
Suspicion	2	4.4
Histrionic	1	2.2
Excessive concern with bodily functions	6	13.3
Depressive thoughts	6	13.3

TABLE IV
Seizure type study (excluding items for which there was insufficient data to analyse)

	N	*T*	*P*
Total scores	12	22.5	NS
Total scoring 2 or more	11	19	NS
Reported symptoms			
Somatic symptoms	8	15.5	NS
Fatigue	8	10.5	NS
Irritability	11	13.5	0.05*
Lack of concentration	6	2	0.047*
Depression	8	12.5	NS
Anxiety	10	25	NS
Phobias	7	16.5	NS
Obsessions	11	30.5	NS
Manifest abnormalities			
Depressed	8	2.5	0.02*
Slow	6	2	0.07*
Excessive concern with bodily functions	8	13.5	NS
Depressive thoughts	5	4.5	NS

n = the number of pairs left after those scoring the same for each item were discarded.
*Scrutiny of the raw data shows that patients with temporal lobe epilepsy were scoring more highly on these items.

TABLE V
Medication study (excluding items for which there was insufficient data to analyse)

	N	*T*	*P*
Total scores	16	59	NS
Total scoring 2 or more	13	34	NS
Reported symptoms			
Somatic symptoms	6	9.5	NS
Fatigue	12	30.5	NS
Sleep disturbance	6	0	0.05*
Hypnotics	3	0	N too small†
Irritability	7	14	NS
Lack of concentration	12	30	NS
Depression	9	21	NS
Anxiety	7	14.5	NS
Phobias	6	6	NS
Obsession	12	33.5	NS
Manifest abnormalities			
Depressed	10	27.5	NS
Anxious	8	17	NS
Flattened	6	9	NS
Excessive concern with bodily functions	12	38	NS

†all patients taking a hypnotic were on carbamazepine.
n = the number of pairs left after those scoring the same for each item were discarded.
*Scrutiny of the raw data shows that it was the carbamazepine group which scored more highly on this item.

type and medication studies respectively. Patients with temporal lobe epilepsy were significantly more likely to complain of irritability and lack of concentration, and significantly more likely to be rated as depressed and slow, than their matched counterparts with tonic-clonic seizures. Patients taking CBZ as sole treatment for their epilepsy were significantly more likely to complain of sleep disturbance than patients taking DPH alone, and while no patient taking DPH was found to have used a hypnotic in the last week, three patients on CBZ had done so. Apart from this, patients on DPH alone did not complain significantly more than patients taking CBZ of any of the other symptoms covered in the questionnaire.

Discussion

The finding that 42% of patients complained significantly of fatigue suggests a higher prevalence of this symptom in our population of out-patients with epilepsy than would be expected in non-medicated or non-epileptic populations, although normative data are lacking. The occurrence of somatic and obsessional symptoms, depression, and anxiety in approximately a quarter of patients may not however be a particularly high figure for a general hospital out-patient population (Jenkins, personal communication). The high reported level of fatigue, independent of type of seizure or medication, is in accordance with the findings of Brown & Tomlinson (1982), who found that epileptic patients complained of this symptom to a significantly greater degree than normal subjects and attributed it to their medication.

There was no overall difference in morbidity between temporal and tonic-clonic subjects, but those with temporal lobe epilepsy were significantly more likely to complain of irritability and lack of concentration, and significantly more likely to be rated as depressed and slowed up. Since these patients did not themselves complain of being more depressed, the apparent observed depression may be in part a halo effect from the slowed-up appearance which was noted, although the difference in observed depression was greater than the difference in observed slowness (Table IV).

The temporal and tonic-clonic patients have been carefully matched for sex, age, social class, seizure frequency, duration of epilepsy, and drug treatment. Therefore, the overall impression of psychomotor slowing and depression, together with irritability and lack of concentration in the former group may be in keeping with some aspects of the temporal lobe syndrome proposed by many authors (Gibbs *et al*, 1948; Geschwind, 1978; Bear *et al*, 1982; Trimble, 1983).

The only significant difference between patients on DPH and those on CBZ was that the latter reported more sleep disturbance; three patients on CBZ (but none on DPH) were also taking a hypnotic, which may reflect a more sedative effect of DPH. The failure to show any other differences was to some extent surprising, as comparative psychometric studies of the two drugs in normal subjects (Trimble *et al*, 1980), chronic epileptic patients (Dodrill & Troupin, 1977) and new referrals with epilepsy (Andrewes *et al*, 1984) have consistently shown more impairment with DPH, especially in tests of memory and concentration (Reynolds, 1983b). Furthermore, there have been persistent claims of a 'psychotropic' effect of carbamazepine, which is also advocated in the treatment and prophylaxis of manic-depressive illness (Post, 1982). The difference between the results from out patients' subjectively reported symptoms and those reported from objective psychometric testing may indicate that the discrete difference between DPH and CBZ detectable in the laboratory are of relatively less consequence to the patients than their self-perception of performance in everyday life. Alternatively, the standardised interview used in this study may lack sensitivity in the areas most relevant to these side-effects. It should be noted, however, that the mean CBZ blood level in the present study was well within the therapeutic range, whereas that for DPH was slightly below the equivalent range.

Epileptic patients are a heterogeneous group, in which multiple biological and psychosocial factors contribute to psychological disability. We examined two separate biological factors—seizure type and type of medication—by controlling other factors as carefully as possible, and by studying less selected patients with relatively well controlled epilepsy attending a neurological clinic. Further studies of these and other factors in larger numbers are indicated to clarify this complex field.

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S. W. Brown, MA, MRCPsych†, *Research Registrar*, †*Current post: Consultant, The David Lewis Centre for Epilepsy, Warford, Nr. Alderley Edge, Cheshire SK9 7UD.*

M. E. L. McGowan, MB, BCh, MRCPsych, *Research Registrar.*

*E. H. Reynolds, MD, FRCP, FRCPsych, *Consultant Neurologist.*

University Department of Neurology, Institute of Psychiatry and Kings College Hospital Medical School, London SE5.

*Correspondence

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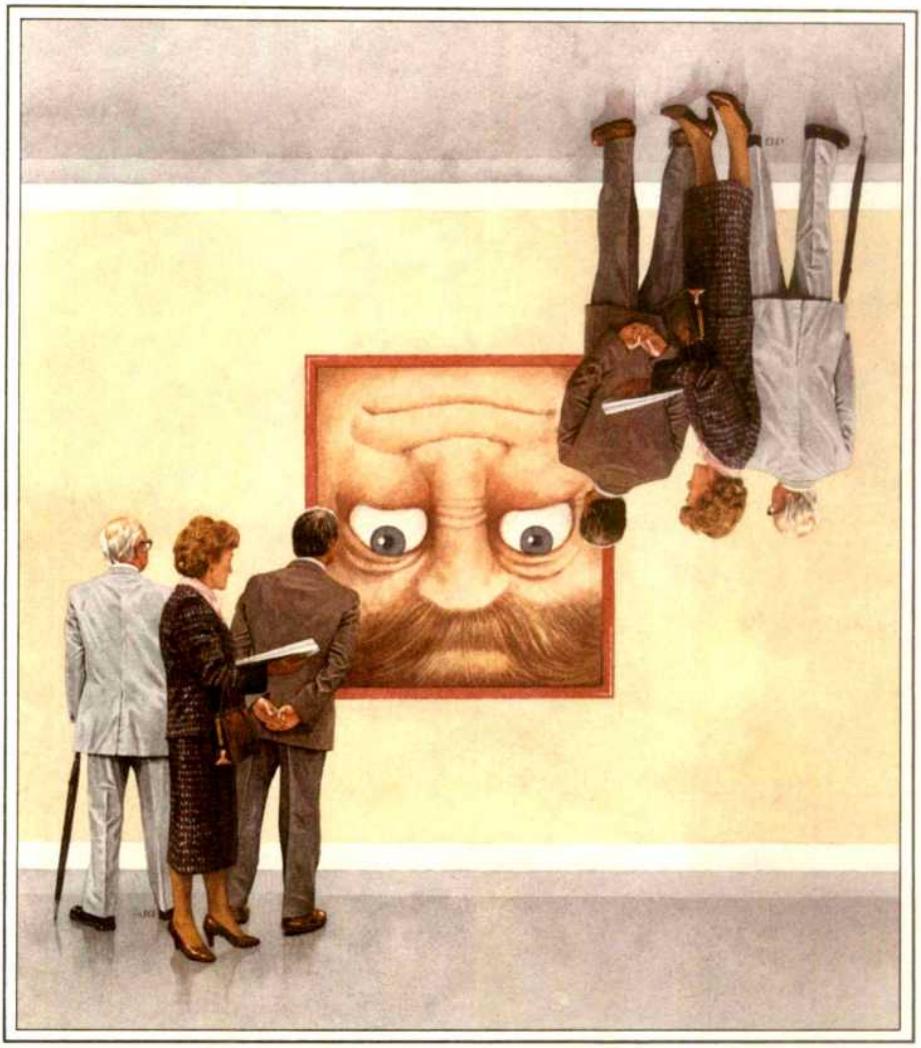

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Cross-national Invariance of Dimensions of Parental Rearing Behaviour:

Comparison of Psychometric Data of Swedish Depressives and Healthy Subjects with Dutch Target Ratings on the EMBU

WILLEM A. ARRINDELL, CARLO PERRIS, HJÖRDIS PERRIS, MARTIN EISEMANN, JAN VAN DER ENDE and LARS VON KNORRING

A psychometric study on Swedish and Dutch samples used the EMBU, a self-report instrument designed to assess memories of parents' rearing behaviour. Of the four primary factors identified previously with Dutch individuals (Rejection, Emotional Warmth, Overprotection, and Favouring Subject), the first three were retrieved in a similar form in the two Swedish groups (depressives and healthy, non-patients). Examination of the metric equivalence of the scales and the strength of the factors for each group indicated that comparisons of patterns and levels between groups from the respective countries on the three factors showing cross-national constancy would be warranted. Scale-level factor analyses of these dimensions produced identical two-factor compositions (CARE and PROTECTION) across national groups which further supported this conclusion.

Family factors, unquestionably influenced by social and cultural forces, are part of the background of many forms of psychiatric illness. Recently, it has been shown empirically that a disturbed childhood background marked by fear and hostility (as products of parental instability) "must ... be considered a potent factor predisposing to psychiatric illness, though the effect is not specific regarding diagnosis" (Hassanyeh *et al*, 1983). Sanua (1980) contends that "the culture moulds the family, and the family moulds the individual".

The difficulties of comparing the family backgrounds of samples of patients in various countries, or even within the same country, are increased by differences in child-rearing methods. The present study was part of a larger project, investigating these methods in many national groups with a cross-cultural model (Berry, 1979); its aim was to provide data about one of the fundamental issues which arise when the model is used in search of comparability between groups viz—whether the data from the national groups under comparison share some common base-line; i.e. whether there is comparative dimensionality (Eysenck & Eysenck 1983). It cannot be assumed that the same items comprising a factor's dimension will be found to share common variance, when different national groups are being studied, and the assumption that they do so must be empirically verified (Eysenck & Eysenck, 1983).

By means of these studies, we hope to transport present understanding of child-rearing practices (knowledge, hypotheses, and laws) to other cultural/national settings, and to test their applicability and generalisability. This coincides with one of several attempts that have been proposed to formulate the goal of cross-cultural psychology (Berry & Dasen, 1974).

We aimed to investigate the degree of generalisability of dimensions of parental rearing behaviour which were identified previously in Dutch samples (Arrindell *et al*, 1983). The degree to which depressed or healthy (non-patient) subjects from Sweden agreed with Dutch subjects in terms of their respective definitions of parental rearing constructs was studied by an objective technique of factorial invariance. This study is strictly psychometric and no attempt was made to examine or explain pattern and/or level differences between the samples on the concerning constructs.

Method

Subjects

Analyses were conducted on data from four samples: 1) 205 Swedish healthy subjects (118 males and 87 females with a mean age of 24.93 years; s.d. = 8.65 years); 2) 141 Swedish depressed inpatients (53 males and 88 females with a mean age of 45.92 years; s.d. = 13.13 years). The diagnostic groups considered were: "unipolar" ($n=47$), "bipolar" ($n=21$), and "neurotic-reactive" ($n=34$). In addition, an "unspecified depressive" group ($n=39$) was also included. (The respective definitions used for defining these categories correspond to those given by Perris (1975)); 3) 277 Dutch healthy subjects (137 males and 140 females with a mean age of 41.07 years; s.d. = 12.54 years); and 4) 841 Dutch phobics, predominantly agoraphobics, with none of the subjects being inpatients (171 males and 670 females with a mean age of 42.18 years (s.d. = 12.21 years)).

The EMBU

The EMBU (*Egna Minnen av BarndomsUppfostran*) is an 81-item · self-report inventory, originally devised in Sweden, which comprises 14 *a priori* aspects of parental rearing behaviour: abusive, depriving, punitive, shaming, rejecting, over-protective, over-involved, tolerant, affectionate, performance-orientated, guilt engendering, stimulating, favouring siblings, and favouring subject (Perris *et al,* 1980). Items are scored on four-point continua (one to four) for each of one's parents.

Factor analytical research with the EMBU in the Netherlands (Arrindell *et al,* 1983) identified four conceptually clear factors which were termed Rejection, Emotional Warmth, Over-protection, and Favouring Subject. In a subsequent study (Arrindell & van der Ende, 1984), the above factors, originally obtained with the phobic sample, were shown to be replicable across split samples of phobics and invariant across distinct populations (phobics *vs* healthy subjects).

Statistical analyses

A technique of factorial invariance, statistically too complex to be described here in full (ten Berge, 1977), was employed. Such a technique makes it possible to interpret similarity between sets of factors—derived for identical items from different populations—in terms of indices of factor comparison (Tucker's coefficient of congruence Φ). Tucker's Φ—the best measure of factorial invariance available (ten Berge, 1977)-ranges from -1.00 through 0 to $+1.00$ (perfect similarity). A criterion of 0.80 was employed for similarity since Haven & ten Berge (1977) have empirically shown that factors for which calculated coefficients have been found to be 0.80 and larger tend to be judged as similar.

In all comparisons, the degree of match between non-corresponding factors was also examined. Preferably, Φ values below $|\pm 0.70|$ should be obtained for these factors on two grounds: a) Φ's<0.70 indicate "terrible" match; and b) Φ's$\cong 0.70$ are frequently produced in comparisons involving factors derived from factor analyses of random data.

The actual rotational procedures have been outlined in detail by Arrindell & van der Ende (1984) and will not be repeated here. The Swedish factor structures were rotated to the corresponding structures of their Dutch counterparts, i.e. the Target (T) of the mothers (TM) and the Fathers (TF). In the light of the higher number of the Dutch phobic sample, compared to that of the healthy sample, the factored ratings of the former were taken as target ratings; greater numbers are likely to make for more reliable results.

Other supplementary analyses, by national group, include the calculation of item-remainder associations by scale, alpha coefficients reliabilities for each scale, determination of the relative strength of the factors (in terms of explained variance), and scale correlation with sex and age. Item-remainder correlations provide a means of assessing the quantitative identity of metric scales across samples. Absence of item-bias can be taken as a condition for comparability. Further, item-analysis serves the function of improving scales for "new" national groups by identification and elimination of undesirable items.

Results and Discussion

The analyses are based on sample numbers that differ slightly from those given in the Method section due to missing data on certain items. The results obtained by substituting the missing data by the grand mean of the remaining sample so as to obtain the original sample numbers are identical to those produced without treatment of the missing values.

Descriptive statistics for individual items were such that no "difficulty factors" could be expected to emerge in any of the factor analyses performed.

Table I sets out the indices of factor comparison for two cross-national comparisons for the ratings of the mothers and the fathers separately: firstly, Swedish healthy subjects and secondly, Swedish depressives versus Dutch phobic Target. Comparisons were made for the sexes combined.

The indices are satisfactory ($\Phi \geq 0.84$) for all factors, with the exception of the values of the Favouring Subject (FS) factor ($0.67 \leq \Phi < 0.80$). The highest off-diagonal coefficient obtained was smaller than 0.7.

Internal consistency coefficients (Cronbach's α) for the Rejection, Emotional Warmth, Over-protection, and FS scales were found to be very satisfactory, as were the corresponding item-remainder associations, which hovered between 0.4 and 0.7. Cronbach's α's for the Swedish group of healthy subjects were for Rejection 0.92 (M) and 0.89 (F), Emotional Warmth 0.90 (M) and 0.92 (F), Over-protection 0.87 (M) and 0.84 (F), and FS 0.77 (M) and 0.74 (F). The corresponding figures for the Swedish depressed sample were for Rejection 0.91 (M) and 0.94 (F), Emotional Warmth 0.93 (M) and 0.92 (F), Over-protection 0.82 (M) and 0.83 (F), and FS 0.73 (M) and 0.76 (F). The corresponding figures for the Dutch groups are given in Arrindell *et al* (1983).

Comparisons of the item-remainder correlations with those obtained with the Dutch data disclosed great similarities in terms of the degree of associations which each correlation denoted. This conclusion, however, did not hold for the FS scale: in the Swedish groups, the item-remainder correlations were found to be in general significantly lower ($P \leq 0.05$) and of smaller magnitude than the ones obtained for the Target group.

Further convergence in results was observed in the relative strength of the separate factors across samples.

TABLE I

Indices of factor comparison (Tucker's Φ) between EMBU ratings of Swedish healthy subjects and depressives, on the one hand, and Dutch TARGET (phobic) ratings ($n \doteq 841$) on the other

M factors	*Dutch phobics, M factors*				
	I	II	III	IV	
Swedish healthy subjects	0.93	0.93	0.95	0.77	(0.21)
Swedish depressives	0.93	0.91	0.84	0.78	(0.22)
F factors	*Dutch phobics, F factors*				
	I	II	III	IV	
Swedish healthy subjects	0.94	0.94	0.95	0.79	(0.20)
Swedish depressives	0.95	0.94	0.85	0.67	(0.23)

M = Mother, F = Father

The means of the off-diagonal coefficients have been placed between parentheses (highest off-diagonal coefficient is smaller than 0.7). I = Rejection, II = Emotional Warmth, III = Over-protection, IV = Favouring Subject. Swedish healthy subjects $n = 205$, Swedish depressives $n = 141$

These figures are not displayed here, but are available on request, from the senior author.

On the basis of the above findings, it was found justifiable to exclude the FS dimension from further analyses.

Correlations among sub-scales and their associations with sex and age

The associations between sub-scales, on the one hand, and sex and age, on the other, will be considered first. Due to the large number of correlations involved ($k = 32$), the Bonferroni inequality (Grove & Andreasen, 1982) was employed to obtain a conservative alpha level ($\alpha_{\text{overall}} = 0.20$). With α_i set at 0.006, age correlated negatively, lowly with the Fathers' and the Mothers' Rejection scales in the Swedish depressed sample (r's $= -0.23$ and -0.27 respectively). These associations point to slightly higher scores for younger depressed subjects (two-tailed tests).

The associations reported for these Swedish samples (like those given previously for Dutch phobics and healthy subjects (Arrindell *et al*, 1983)) are mostly negligibly low (i.e., < 0.10)—so low that they may be considered to be of little, if any, practical relevance.

Another source of validation is to examine the correlations among the sub-scales in the Swedish samples. These figures offer the opportunity of checking the similarity of results from the different samples by looking at differences found in these groups.

The following associations were found for the Swedish samples: 1) Rejection correlates, at least moderately, positively, with Over-protection, in both the Mothers' and the Fathers' data (0.56 (M) and 0.48 (F) in the healthy subjects, and 0.57 (M) and 0.60 (F) in the depressed sample), which is in keeping with Parker *et al*, (1979); and 2) Emotional Warmth correlates, at least moderately, negatively, with Rejection (-0.50 (M) and -0.52 (F) in the healthy group, and -0.51 (M) and -0.39 (F) in the depressed group) ($P \leqslant 0.001$, one-tailed test). These figures are comparable to those reported for the Dutch samples. However, to put this comparison on a somewhat more quantitative footing, indices of factor comparisons were calculated.

First, of course, the matrices of correlations had to be factor analysed (as in our previous work) for each of the samples, including both M and F scales. Following an invariance procedure identical to the one described in Arrindell & van der Ende (1984), the Φ coefficients were produced given in Table II. This portrays the factor structures, the percentage variance explained by each rotated factor, and the labels given to each. (Figures are included for both Dutch phobics and Dutch healthy subjects.)

It will be seen that two factors with eigenvalues exceeding unity emerged for all four samples; and that while both factors could be interpreted uniformly, namely as CARE (Emotional Warmth *vs* Rejection) and PROTECTION, they were found to be comparatively strong across samples as well.

Very high Φ coefficients (≥ 0.99) were obtained in the comparisons made between the correlational structures of Dutch healthy subjects, Swedish healthy subjects and Swedish depressives, on the one hand, and that of Dutch phobics, on the other. The Φ values clearly indicate that the correlational and factorial structures described are virtually identical, which is another powerful argument for assuming equivalence of the present scales across countries.

TABLE II

Factor analyses of certain EMBU scales (M and F) by subject group; the variance explained by each (rotated) factor and the degree of match between analogous factors in comparing Dutch healthy subjects, Swedish healthy subjects and Swedish depressed subjects with Dutch TARGET (phobic) sample*

	*Dutch phobics**		*Dutch healthy subjects*		*Swedish healthy subjects*		*Swedish depressives*	
	C	*P*	*C*	*P*	*C*	*P*	*C*	*P*
Father								
Rejection	−0.65	0.45	−0.68	0.49	−0.67	0.51	−0.52	0.65
Emotional Warmth	0.88	0.12	0.89	0.20	0.89	0.13	0.93	0.16
Over-protection	0.01	0.90	0.04	0.89	−0.03	0.89	−0.11	0.87
Mother								
Rejection	−0.70	0.44	−0.62	0.48	−0.62	0.54	−0.66	0.57
Emotional Warmth	0.89	0.07	0.90	0.17	0.89	0.10	0.93	0.14
Over-protection	−0.06	0.86	0.01	0.88	−0.14	0.89	−0.17	0.82
PV**	41.22	32.82	40.90	35.23	40.53	35.88	41.17	36.93
Φ			1.00	1.00	1.00	1.00	0.99	0.99
Φ_2			−0.17		−0.24		−0.26	

*The original "unrotated" Varimax rotated Dutch phobic structure has been displayed. Therefore, the presented per cent variance explained for each factor in this sample corresponds with the per cent variance explained for each *unrotated* factor

**PV = per cent variance explained by each *rotated* factor = (sum of squared factor loadings/6) × 100%

C = CARE, P = (Over-) PROTECTION; Φ_2: mean value of the off-diagonal coefficients; highest off-diagonal coefficients: $< |0.30|$

Dutch phobics $n = 841$, Dutch healthy subjects $n = 277$, Swedish healthy subjects $n = 205$, Swedish depressives $n = 141$

All cross-cultural comparisons suffer from the difficulty of discovering whether measures applied in one country carry the same meaning in another (Saklofske & Eysenck, 1978). The results of this study establish fairly clearly that three out of the four factors which originally emerged from an analysis of the intercorrelations of questionnaire items on aspects of parents' rearing behaviour and attitudes in Dutch phobic and healthy (non-patient) subjects were identified in a similar form in the samples of Swedish healthy subjects and depressed patients. Rejection, Emotional Warmth, and Over-protection are as clear-cut and interpretable in the Swedish culture as they are in the Dutch; i.e. the dimensions give evidence of clear cross-national generalisability. Reliabilities, inter-scale correlations and other properties of these scales are very similar to those obtained for Dutch samples and point also to metric equivalence of the scales (across the present national groups). On the basis of these constancy aspects, it can be concluded, for practical purposes, that the same descriptive three-factor framework is sufficient to permit measurement in the countries under consideration, and that future comparisons are permissible between the countries in terms of their mean scores on the three EMBU dimensions in question (Saklofske & Eysenck, 1978; Eysenck & Eysenck, 1983).

It should be noted that the lack of invariance of the Favouring Subject factors may be due to two aspects. In the light of the results of the present analyses, the most obvious explanation for this lack is the difference between nations in the meaning of the items captured by the corresponding scale. A second observation which should not be overlooked is that in the Arrindell *et al* (1983) study, the FS factor explained only 3.8% of the total variance in both the phobic M and F ratings, which is only about 9% of the variance extracted using all four factors. This small amount of variance coincides with that found in each of the Swedish samples for the FS factor. Such small factors are rather difficult to replicate.

Assuming that the content validity of the EMBU is satisfactory (the careful methods followed in selecting items for the *a priori* scales by Perris *et al* (1980) and a content analysis by Arrindell & van der Ende (1984) point in this direction), the scale-level factor analyses conducted here support a two-factor model of parental rearing behaviour—CARE and PROTECTION (Parker *et al*, 1979).

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*Willem A. Arrindell, *Clinical Psychologist, Department of Clinical Psychology, Academic Hospital of the State University of Groningen, Oostersingel 59, 9713 EZ Groningen, The Netherlands.*

Carlo Perris, MD, *Professor of Psychiatry and Chairman, Department of Psychiatry III and WHO Collaborating Centre for Research and Training in Psychiatry, Umeå University, S–901 85 Umeå, Sweden.*

Hjördis Perris, PhD, *Associate Professor of Medical Psychology, Department of Psychiatry, Umeå University.*

Martin Eisemann, PhD, *Research Psychologist, Department of Psychiatry, Umeå University.*

Jan van der Ende, *Research Psychologist, Department of Clinical Psychology, Academic Hospital, Groningen.*

Lars von Knorring, MD, *Associate Professor of Psychiatry, Department of Psychiatry, Umeå University.*

*Correspondence

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Mortality and Facial Dyskinesia

H. A. McCLELLAND, D. DUTTA, A. METCALFE and T. A. KERR

In 1965 a psychiatric in-patient population was surveyed for the prevalence of facial dyskinesia. The present investigation reports on their survival time. Among male and female patients with functional disorders (mostly schizophrenia) there was a strong association between *moderate* or *severe* facial dyskinesia and shortened survival, but no clinical factors were found to explain this. *Mild* facial dyskinesia in functional disorders was not associated with reduced life expectancy and may be attributable to the general effects of ageing rather than to a specific pathological process. Among patients with primary organic brain syndromes, dyskinesia was not associated with reduced life expectancy.

With tardive dyskinesia, clinicians are concerned over disfigurement and disability, but an association with premature death is rarely considered. Two studies that have analysed the life expectancy of patients with dyskinesia have produced contradictory findings. Mehta *et al* (1978) did a five-year prospective study of 35 patients with dyskinesia and 35 without, matched for age, sex and diagnosis (functional psychosis, organic brain syndrome, and mental retardation). They found that the patients with tardive dyskinesia died significantly earlier than the controls ($P<0{\cdot}05$). In contrast, Kucharski *et al* (1979), in a follow-up study of 377 patients with schizophrenia and organic brain syndrome, found no significant association between dyskinesia and early death, although the length of follow-up was only 18 months and only 16 patients had died.

In 1965 a prevalence study of facial dyskinesia was carried out on in-patients of St. Nicholas Hospital, Newcastle-upon-Tyne (Brandon *et al*, 1971). Fifteen years later we initiated a follow-up study with the aim of determining outcome, including life expectancy. The present paper compares the survival time of patients with and without facial dyskinesia; it also reports on an attempt to identify clinical features related to degree of dyskinesia and survival time. Our working hypothesis was that psychiatric patients with dyskinesia had an associated neurological disorder which would shorten survival time.

The 1965 study

The 1965 survey was carried out on all 910 medium- and long-stay patients of the hospital, all of whom were examined at least twice. The overall prevalence of facial dyskinesia was 24% (30.5% in the 484 females, 15.3% in the 426 males). There was no appreciable difference in dyskinesia rates between those with organic and those with functional diagnoses. Among the women, 13.4% had mild dyskinesia and 15% had moderate or severe dyskinesia, with the comparable rates for men being 9% and 4%. In each sex 2% were rated as having doubtful dyskinesia but were included in the "mild" category in subsequent analyses. The association between neuroleptics and facial dyskinesia was weak, with 25% of the dyskinetic patients never having been prescribed neuroleptics. However, a pertinent criticism of the study is that the analyses did not take into account the grades of dyskinesia.

Follow-up Study A: Survival Time of Females

Method

Of the 1965 female in-patient population of 484, the outcome in terms of age at death or age at survival was traced for 408 (84%) up to December 1983. This cohort included patients who had been discharged from hospital since 1965. For each patient, we extracted from the 1965 research records information on dyskinesia status (nil/mild/moderate/severe) and hospital diagnosis, classified in the first instance as "functional disorder" or "organic brain syndrome".

The analysis of the effect of dyskinesia on survival time was based on the Cox proportional hazards regression model (Cox, 1972) which presumes that death rates may be modelled as log-linear functions of the covariates (see Appendix). The co-variates in our analyses were: age in 1965, degree of dyskinesia and psychiatric diagnosis. Discriminant function analysis was used to investigate evidence of any association between dyskinesia status and diagnosis.

All analyses examining the relationship of survival time to dyskinesia used one-tailed P values, i.e. the null hypothesis that dyskinesia does not shorten survival time was tested against the alternative that it does. This was appropriate as dyskinesia, being a neurological disorder, would

TABLE I

Study A: Degree of dyskinesia and age (in 1965) of the 408 female patients traced at follow-up in December 1983

	Functional disorder (n=249)	*Organic disorder (n=159)*
Dyskinesia status (1965)		
Absent	172(69%)	102(64%)
Mild	37(15%)	17(11%)
Moderate	34(14%)	34(21%)
Severe	6(2%)	6(4%)
Age in 1965		
Range	20.0–89.0	29.0–92.0
Mean ± s.d.	61.2 ± 15.0	72.4 ± 13.3

not *increase* longevity. Similarly, one-tailed values were found when examining the effect of age. All other *P*-values given are two-tailed.

Results

The 1965 female in-patients traced comprised 249 cases of functional disorder and 159 cases of organic brain syndrome: 31% of the "functional" patients and 36% of the "organic" patients had some degree of facial dyskinesia (Table I). Table I also shows the wide age-range of the group in 1965. By 1983 only 88(35%) of those with functional disorders and 9(6%) of those with organic disorders were still alive.

Functional disorders

The frequencies of the different functional disorders in 1965 were as follows:

184 cases of schizophrenia
51 cases of manic–depressive psychosis
1 case of schizo-affective disorder
13 cases of "other" functional disorders (neuroses and personality disorders).

Discriminant function analysis produced some evidence of an association between manic–depressive psychosis and absent/mild dyskinesia, once age and survival time were allowed for ($P<0\cdot025$).

In our analysis of survival time, the dependent variable was "death rate" and the covariates were:

1. Age in 1965
2. Mild/moderate/severe dyskinesia (tested against absence of dyskinesia)
3. Manic–depressive psychosis/"other disorders" (tested against schizophrenia)

If a covariate in such an analysis is found to have a statistically significant effect on the death rate this can be interpreted as a significant effect on the mean (or median) survival time.

The results of the analysis are given in Table II. As expected, age was very significantly associated with reduced survival. There was no evidence that *mild* dyskinesia was associated with reduced survival time, but the associations of moderate and severe dyskinesia with shortened survival time were both highly significant. Patients with a diagnosis of manic–depressive psychosis had significantly reduced survival times compared with schizophrenics, irrespective of dyskinesia status.

TABLE II

Study A: Analysis of associations between survival time and age, degree of dyskinesia and diagnosis: results of fitting proportional hazards model to patients with (a) functional disorders, and (b) organic disorders. P-values are based on the likelihood-ratio test: they are one-tailed for the age and dyskinesia variables, two-tailed for diagnostic variables

Covariate	*Functional disorders (n=249)*			*Organic disorders (n=159)*		
	Coefficient	*Standard error*	*P-value*	*Coefficient*	*Standard error*	*P-value*
Age in 1965	0.064	0.008	<0.0005	0.0184	0.0113	0.050
Mild dyskinesia[1]	−0.072	0.227	0.625	−0.0422	0.2731	0.561
Moderate dyskinesia[1]	0.569	0.213	0.005	0.2920	0.2037	0.080
Severe dyskinesia[1]	1.119	0.432	0.012	0.1640	0.4678	0.366
Manic–depression[2]	0.487	0.188	0.012			
Other functional diagnoses[2]	0.049	0.429	0.910			
Multi-infarct dementia[3]				−0.0891	0.2242	0.689
Other chronic organic brain syndromes[3]				−0.5242	0.3532	0.132

[1] Compared with absence of dyskinesia
[2] Compared with schizophrenia
[3] Compared with Alzheimer-type dementia

Organic disorders

The categories of organic disorders ($n = 159$) were:

- 92 cases of Alzheimer-type dementia
- 28 cases of multi-infarct dementia
- 39 cases of other organic disorders (including Huntington's chorea, neurosyphilis and head injury)

We found no evidence of any association between diagnostic category and degree of dyskinesia.

The covariates considered in the Cox model of survival time were:

1. Age in 1965
2. Degree of dyskinesia
3. Multi-infarct dementia/other organic brain syndromes (tested against Alzheimer-type dementia)

As Table II shows, age was found to be only marginally significant, indicating that the serious pathology of coarse brain syndromes overrides the effect of shortened life expectancy due to increasing age. Degree of dyskinesia was not significantly associated with shortened life expectancy, nor were particular organic diagnoses.

Conclusions

These findings can be illustrated by giving the median survival time for a female patient aged 61.2 years. If such a patient had an organic brain syndrome then her life expectancy would be 2.4 years irrespective of her dyskinesia status. If the diagnosis was that of a functional illness then her life expectancy would be 13.4 years if dyskinesia was absent or mild but only 10.6 years if moderate or severe dyskinesia was present.

Follow-up Study B: Deaths in Hospital

Method

Of the 484 female and 426 male subjects of the 1965 study, 311 females and 279 males had died in hospital by June 1982. For each patient who had died we recorded their survival time from 1965, their dyskinesia status in 1965, and the hospital psychiatric diagnosis. Statistical analyses of survival time were performed using the Cox model.

We were aware that a sample restricted to patients who had died in hospital could be biased. Furthermore, analysis had to allow for the fact that since only patients who died within 17 years were considered the effect of age in 1965 on survival was likely to be complex. Despite these reservations we consider this study to be of value since it allows the effect of sex to be considered.

Results

Of the patients who died in hospital, 122 females (39%) and 50 males (18%) had shown some degree of dyskinesia in 1965. Table III shows the numbers with functional and organic disorders, their dyskinesia status, survival time from 1965, and mean age at death. Table IV gives details of dyskinesia status in different age-groups in 1965. Of the 334 patients with functional disorders, 249 suffered from schizophrenia and 73 from manic–depressive psychosis, while 12 had other diagnoses. Dyskinesia was twice as common in females and markedly more common among the elderly. Overall there was an almost equal prevalence of facial dyskinesia in the "functional" and the "organic" groups.

The prevalence of dyskinesia tended to increase with age, although this relationship was most striking for the mild forms of dyskinesia (Table IV). The frequency of mild dyskinesia increased greatly in the 61–70 age-group, in both sexes and both major diagnostic groups, with a further large increase in the 70+ age group: of 74 cases of mild dyskinesia only 29 (39%) occurred in those aged 70 years or under. By contrast, 55 of the 98 cases of moderate and severe dyskinesia (56%) were patients under the age of 70 years ($\chi^2 = 4.8$, $P < 0.05$).

Cox analyses of survival time were performed on the

TABLE III

Study B (patients who died in hospital, 1965–1982): survival time and age at death compared with diagnosis and degree of dyskinesia in 1965

Dyskinesia status (1965)	*Number of patients*		*Mean survival time (years)*		*Mean age at death (years)*	
	Males	*Females*	*Males*	*Females*	*Males*	*Females*
Functional disorders ($n = 334$)						
Absent	142 (82%)	95 (59%)	7.1	7.2	70.3	72.8
Mild	19	28	5.7	7.2	75.4	78.2
Moderate	9	32	5.9	5.9	66.3	76.4
Severe	3	6	9.7	4.0	68.0	70.0
Present (all grades)	31 (18%)	66 (41%)	6.2	6.3	72.1	76.6
Organic disorders ($n = 256$)						
Absent	87 (82%)	94 (63%)	4.0	2.4	70.7	77.7
Mild	11	16	2.5	2.2	77.8	75.9
Moderate	8	34	4.2	2.5	67·6	72·4
Severe	0	6	—	2.8	—	76.5
Present (all grades)	19 (18%)	56 (37%)	3.3	2.4	73.5	73.3

TABLE IV
Study B: Numbers of patients with dyskinesia of different degrees of severity in different age-groups

Age in 1965	*Patients with functional disorders (n=334)*					*Patients with organic disorders (n=256)*				
	Nil	*Mild*	*Moderate*	*Severe*	*(Total)*	*Nil*	*Mild*	*Moderate*	*Severe*	*(Total)*
Males (n=279)										
Under 50	22	0	3	0	25 (14.5%)	11	0	0	0	11 (10.4%)
50–59	28	3	0	2	33 (19.1%)	13	0	3	0	16 (15.1%)
60–69	53	7	5	0	65 (37.6%)	24	4	5	0	33 (31.1%)
70 and over	39	9	1	1	50 (28.9%)	39	7	0	0	46 (43.4%)
Total	142 (82.1%)	19 (11%)	9 (5.2%)	3 (1.7%)	173 (100%) (100%)	87 (82.1%)	11 (10.4%)	8 (7.5%)	0 (0%)	106 (100%) (100%)
Females (n=311)										
Under 50	9	2	1	1	13 (8.1%)	4	1	4	0	9 (6.0%)
50–59	19	0	5	1	25 (15 5%)	8	1	2	0	11 (7.3%)
60–69	32	8	9	2	51 (31.7%)	10	3	9	3	25 (16.7%)
70 and over	35	18	17	2	72 (44.7%)	72	11	19	3	105 (70.0%)
Total	95 (59%)	28 (17.4%)	32 (19.9%)	6 (3.7%)	161 (100%) (100%)	94 (62.7%)	16 (10.7%)	34 (22.7%)	6 (4%)	150 (100%) (100%)

"functional" and "organic" groups separately, the covariates being age, sex and grade of dyskinesia (nil/mild/moderate/severe). The results were similar to those of study A and sex was not found to be a differentiating feature. In the "functional" group shortened survival time was significantly associated with moderate dyskinesia ($P<0{\cdot}05$) and weakly with severe dyskinesia ($P<0.1$): the effect of mild dyskinesia was negligible. In the organic group there was no apparent effect of dyskinesia of any severity on survival time.

Follow-up Study C: Clinical Features and Survival Time

Method

To identify other variables that might be related to survival time, biographical and clinical data were culled from the research records and hospital notes of 222 female patients (110 with functional and 112 with organic disorders), these being a random sample of those who had died in hospital since 1965. Data were obtained on:

1. Types of significant physical illness/disability on admission and in the year preceding death.
2. Number of falls/fractures, episodes of restlessness or delirium and infections in the 12-month and 3-month periods preceding death.
3. Treatment history:
   (a) The types of neuroleptic prescribed over the years.
   (b) An estimate of the mean daily dose (expressed in chlorpromazine equivalents), between 1965 and the time of death. This was calculated by taking the average of the daily dose at the time of the 1965 survey and the amounts prescribed on one day chosen at random in each of the years 1970, 1975 and 1980.
   (c) Number of drug holidays; whether on neuroleptics continuously; sedative neuroleptics only (chlorpromazine, thioridazine); or free of neuroleptics in the 12 months prior to death.
4. Whether on benzodiazepines or antidepressants at the time of death.
5. The number of electroconvulsive treatments, and whether insulin coma was used or psychosurgery was performed.
6. Length of hospital stay.

On the basis of all the data available, the original hospital diagnoses were revised on the basis of more modern diagnostic concepts based on DSMIII criteria (American Psychiatric Association, 1980), which had the effect of making the diagnosis of "manic–depressive psychosis" more frequent at the expense of schizophrenia.

The Cox regression model, discriminant function analysis and chi-squared tests were used to analyse the data.

Results

As studies A and B had found a significant relationship between dyskinesia and shortened survival time only with functional disorders, further analyses were confined to the 110 female patients with schizophrenia ($n=78$), manic–

depressive psychosis ($n=27$) or other functional disorders ($n=5$).

Cox regression analyses were performed with survival time as the dependent variable, and covariates including dyskinesia status.

As expected, moderate/severe dyskinesia had a highly significant association with *shortened* survival time ($P=0.007$). Two additional variables had a highly significant association with *lengthened* survival, namely length of last in-patient stay ($P<0.001$) and "impaired hearing" ($P<0.001$). "Length of last in-patient stay" also had a highly significant association with schizophrenia. If the variables relating to length of hospital stay were excluded from analysis then the following factors were associated with altered survival time: impaired hearing with longer survival ($P=0{\cdot}013$); manic–depression with shortened survival ($P=0{\cdot}014$); and psychosurgery ($n=8$) with shortened survival ($P=0{\cdot}063$, $r=0{\cdot}06$). (It should be remembered that these three probabilities are given as two-tailed values.) Chi-squared tests found no significant association between these factors associated with survival time and the presence or absence of moderate-to-severe dyskinesia.

Detailed analyses were undertaken of the amount and type of neuroleptics prescribed, but no significant association was found between such treatment and survival time, and none of the other variables tested had any significant association with altered survival time.

Two discriminant function analyses were performed, using dyskinesia status to divide the population. The first analysis, with three groups (dyskinesia absent/mild/moderate or severe), found no features that clearly discriminated. The second analysis considered two groups (dyskinesia absent or mild/moderate or severe) and the discriminant function showed that longer survival ($P<0.025$) and manic–depression ($P<0.05$) were predictors for membership of the "dyskinesia absent or mild" group. In the manic–depressive group 2 out of 27 patients had moderate or severe dyskinesia, compared with 20 out of the 78 schizophrenics. It should be remembered that this ignores survival time and that manic–depressive psychosis is also associated with shorter survival. The small number of manic–depressive patients in study C with moderate or severe dyskinesia could possibly be explained by the effects of neuroleptic prescribing: examining the prescribing data from 1965 onwards showed that 87% of schizophrenic patients were prescribed neuroleptics compared with 63% of other patients, and schizophrenics were also more likely to have been prescribed neuroleptics in large amounts (defined here as over 200 mg CPZ a day, or 400 mg for those under 65). A chi-squared test showed that this neuroleptic prescribing pattern differentiated significantly between the diagnostic groups ($P<0.006$). This explanation would imply that neuroleptics are associated with moderate or severe dyskinesia. The corresponding null hypothesis (no such association) cannot be tested directly, as information on neuroleptic prescribing before 1965 is not available. If the variable "total dose of neuroleptics, 1965 to end of illness" is considered as a proxy then a marginally significant association is obtained: 2 of the 23 patients who had no neuroleptics during this period had moderate or severe dyskinesia, compared with 21 of the 86 patients who did have neuroleptics ($\chi^2=2.7$, $P=0.10$).

A third discriminant function analysis compared the two groups (dyskinesia absent or mild/moderate or severe) as before but excluded psychiatric diagnosis as a variable. In this analysis the groups were further discriminated by the variable "number of infections in the 12 months prior to death": 20 out of the 24 with moderate or severe dyskinesia had had more than one infection recorded, compared with 54 out of 86 in the "dyskinesia absent or mild" group ($\chi^2=3.6$, $P=0.06$). This finding led to us to consider the possibility of an association between infections and neuroleptics. However, there was no evidence for this.

Chi-squared analyses were also performed to determine whether degree of dyskinesia was associated with cause of death or physical disorders such as sensory handicap, deformity, falls/fractures, etc. No significant relationships were found.

Discussion

The present study was confined to *facial* dyskinesia, as this disorder was the subject of the 1965 survey. However, Jeste & Wyatt (1982), summarising various studies, found that 81% of patients with tardive dyskinesia had abnormal oro-facial movements as an essential part of their dyskinesia.

Our study found no association between facial dyskinesia and premature death in patients with primary organic brain syndromes. However, the mean survival time of patients with organic disorders was (predictably) much shorter than that of a comparable group of patients with functional disorders, so any possible effect that dyskinesia might have had in reducing survival time was probably swamped by the effects of the primary general neuropathological process underlying the organic brain syndrome. Among female patients with *functional* disorders, there was a significantly shortened survival time for those with moderate and severe dyskinesia (study A). The results of the analysis in study B also showed a significantly reduced survival time for those with moderate dyskinesia, with a non-significant reduction for those with severe dyskinesia: reduced life expectancy was found in both sexes and in all three categories of functional diagnoses (schizophrenia, manic–depression and "other").

Clinical and research evidence points to the basal ganglia as being the crucial areas affected in tardive dyskinesia. This in itself, however, does not explain the reduced life-expectancy found in the dyskinetic "functional" patients. It is true that such disorders as primary Parkinsonism or Huntington's chorea decrease life span, but they are progressive in a way that only occurs in a minute number of dyskinetic patients. It would be reasonable to suppose that patients with dyskinesia had a greater chance of dying from the consequences of falls and fractures, but we found no evidence to support this supposition.

Other possible causes of shortened survival time for patients with dyskinesia, including physical disorders and drugs, were examined but none could be identified. However, we have some reservations about the quality of our data, which were drawn retrospectively from hospital documents of uncertain reliability. Furthermore, attempts to itemise neuroleptic prescribing are notoriously difficult and our study only sampled prescribing at five-year intervals. It is of interest that the only other study to report reduced survival time (Mehta *et al*, 1978) also failed to find any clearly defined link between dyskinesia and any physical disorder (including neurological abnormality).

Manic–depressive patients had shortened survival times: this finding is now generally accepted (Coryell & Winokur, 1982). In study C, where modern psychiatric diagnostic concepts were applied (the original hospital diagnoses were used in studies A and B), manic–depressive patients were found to have a much lower prevalence of dyskinesia than schizophrenics. This might be explained by postulating that schizophrenic patients have more primary neurological damage which increases their chances of developing dyskinesia, although another factor which clearly distinguished between the two diagnostic groups was neuroleptic prescribing: schizophrenic patients were prescribed neuroleptics more often and were much more likely to have been given large amounts.

We found that minor forms of facial dyskinesia (low-grade oral movements) were not associated with premature death. This is consistent with the view that these movements are not necessarily a minor or early form of tardive dyskinesia (which is a specific neurological syndrome). In fact, patients with minor dyskinesia were most commonly found in the oldest age-groups, suggesting that minor dyskinesia may represent a "normal" ageing process which is unconnected with primary neuropsychiatric disorders or neuroleptic prescribing, but is related to a combination of factors, both peripheral (loose-fitting dentures, decreased salivation) and central (early neuronal degeneration).

In conclusion, this study provides evidence that moderate-to-severe facial dyskinesia is associated with significantly shortened survival times in patients with chronic functional psychoses but not in patients with organic brain syndromes. It is possible that dyskinesia (made overt by neuroleptics) may only be a by-product of a neuropathological process which underlies functional psychoses, particularly schizophrenia (Owens, Cunningham & Johnstone, 1980). Such neuropathology could increase the overall vulnerability of the individual to other disorders and therefore indirectly to early death. It is also possible that other factors such as long-term neuroleptic prescribing, either by themselves or in association with the primary process, may contribute to early death, but this could not be demonstrated in the present study. However, tardive dyskinesia is essentially a neuroleptic-induced disability, and our finding of an increased liklihood of earlier death among patients with facial dyskinesia is a further reason for the constant monitoring of patients on neuroleptics in order to keep the dose down to the minimum required for adequate control of the psychosis.

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Appendix: Cox Proportional Hazards Regression Model

This technique presumes that death rates may be modelled as log-linear functions of the covariates. If $h(t; z)$ is the death rate at time t for individuals with covariate array z, then the proportional hazards model is given by:

$$h(t; z) = h_0(t) \exp(\beta^T z)$$

where $$\beta^T z = \beta_1 z_1 + \ldots + \beta_k z_k$$

where $\beta_1, \ldots, \beta_k$ are the unknown coefficients and $z_1, \ldots, z_k$ are the values of the k covariates for a particular patient. Let $z(i)$ denote the array of the covariates for patient i. Then $h(t; z(i))\,(\delta t)$ is the probability of death in the time interval $(t, t+\delta t)$ given that the patient is alive at time t. If it is given that a patient dies at time $t(i)$, the probability that it is the particular patient i equals

$$\frac{\exp(\beta^T z(i))}{\sum_j \exp(\beta^T z(j))}$$

where the summation is over all patients at risk immediately before $t(i)$. Each death contributes a factor of this nature. The estimate of β is the value which maximises the product of these factors. This method of analysis can be used with data which include survivors.

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*H. A. McClelland, MB, FRCP, FRCPsych, *Consultant Psychiatrist, St. Nicholas Hospital, Gosforth, Newcastle-upon-Tyne NE3 3XT.*

D. Dutta, MB, MRCPsych, *Consultant Psychiatrist, St. Mary's Hospital, Stannington, Northumberland.*

A. Metcalfe, BSc, FSS, *Lecturer, Department of Engineering Mathematics, University of Newcastle-upon-Tyne, Newcastle-upon-Tyne NE1 7RU.*

T. A. Kerr, MD, FRCPsych, *Consultant Psychiatrist, St. Nicholas Hospital, Gosforth, Newcastle upon Tyne NE3 3XT.*

*Correspondence

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Hypothyroidism as a Correlate of Lateral Ventricular Enlargement in Manic-Depressive and Neurotic Illness

EVE C. JOHNSTONE, D. G. C. OWENS, T. J. CROW, N. COLTER, CLAIRE A. LAWTON, R. JAGOE and L. KREEL

Lateral ventricular size, as assessed by computed tomography, was not significantly greater in manic-depressive cases than in neurotic patients, but 19% of manic-depressive cases had ventricular brain ratios (VBR) more than two standard deviations above the neurotic mean. Few correlates of VBR were found in the features of the illness and the treatment given, apart from the fact that in the outpatient sample, there was a significant association between increased VBR and hypothyroidism. Hypothyroidism was relatively common in this sample, but was treated and not associated with cognitive impairment. There was no relationship between lithium administration and VBR.

There has been interest in the findings of brain imaging techniques in patients with psychotic illness over 50 years (Jacobi & Winkler, 1927), but this increased following the introduction of computer-assisted tomography (CT) (Hounsfield, 1973). The main focus of attention has been on schizophrenia, in which lateral ventricular enlargement is the abnormality most frequently noted (Johnstone *et al*, 1976; Weinberger *et al*, 1979), but this change has also been described in affective illness (Pearlson & Veroff, 1981; Nasrallah *et al*, 1982; Rieder *et al*, 1983). In a recent study (Owens *et al*, 1985) where groups of long-stay and discharged patients with schizophrenia and manic-depressive psychosis were compared with outpatients with neurotic illness, lateral ventricular size (in terms of ventricular-brain ratio, VBR) was increased in patients with schizophrenia, by comparison with other diagnostic groups. The values for the patients with affective illness lay between, but did not differ significantly from those of patients with schizophrenia on the one hand and neurosis on the other; 20% of the manic-depressive inpatients and 18.2% of the manic-depressive outpatients had ventricles greater than two standard deviations above the mean of the group of patients with neurosis. The present investigation is concerned with the determinants of ventricular enlargement in the affective sample.

Method

The total CT scan study (Owens *et al*, 1985) involved chronic schizophrenic inpatients, discharged schizophrenics, manic-depressives receiving long-term inpatient care, manic-depressive outpatients, neurotic outpatients, and inpatients with a first episode of schizophrenia. The manic-depressive and neurotic patients were selected to match the sample of 112 schizophrenic inpatients as closely as possible for age and sex. The manic-depressive inpatients were patients of Shenley Hospital who conformed to the St. Louis (Feighner *et al.* 1972) Criteria for primary affective disorder and had been inpatients continuously for more than one year at the time of the investigation; this sample was documented in detail (Johnstone *et al*, 1985), and ten patients were chosen for CT scanning. The manic-depressive and neurotic outpatient groups were drawn from the outpatient case loads of the participating clinicians; they had clinical diagnoses of manic-depressive illness, neurotic depression, or anxiety neurosis. The St. Louis Criteria were applied to the casenotes. For the purposes of the study, those who conformed to the criteria for primary affective disorder were placed in the manic-depressive group, and the remainder in the neurotic group. The patients in the neurotic group either fulfilled the St. Louis Criteria for anxiety neurosis or fell into the category of undiagnosed psychiatric illness—the latter because their symptoms were relatively minor, or they had a mixture of anxiety and depressive features. In the total outpatient sample, historical items, including the number of episodes and admissions, the length of time since onset, physical ill-health since onset, the possibility of alcohol abuse, and years of prescription of tricyclics, other antidepressants, benzodiazepines, other anxiolytics, neuroleptics, and lithium were recorded on a standardised form.

All scans were performed on an EMI 5005 whole body scanner at 120 kv with a scanning time of 65 seconds; full details of the scanning procedure and the method of measuring the scans have been reported elsewhere (Owens *et al*, 1985). Following assessment of the scans of the entire sample (approximately two years after the images had been taken) the outpatients were traced, and their cognitive function assessed using the Withers & Hinton (1971) test battery. The results were calculated using analysis of

TABLE I
Age, sex, and history of alcohol abuse and physical illness in patient groups

Group	*Mean age*	*Sex*	*History of alcohol abuse at any time*	*Physical illness since onset of psychiatric disorder*
Neurotics ($n = 19$)	56.0	9 males 10 females	16—no 2—uncertain 1—yes	13—none 2—hypothyroidism 1—investigated for possible transient ischaemic attacks 1—retinal haemorrhage 1—polymyalgia rheumatica 1—osteoarthritis
Manic-depressive outpatients ($n = 22$)	54.7	11 males 11 females	14—no 5—uncertain 3—yes	12—none 3—hypothyroidism 2—myocardial infarction 1—carcinoma of the breast (12 years ago no recurrence) 1—menorrhagia→hysterectomy 1—thyrotoxicosis→partial thyroidectomy (since euthyroid) 1—chronic bronchitis 1—hypertension
Manic-depressive inpatients ($n = 10$)	65.2	2 males 8 females	not recorded	not recorded

co-variance with age as the co-variate and taking sex into account where possible.

Results

The nature of the sample is shown in Table I.

No significant group differences in VBR were found between the manic-depressive inpatients, the manic-depressive outpatients, and the neurotics, nor was there a significant difference between all manic-depressive groups taken together and the neurotics. All the manic-depressive inpatients were bipolar. Among the outpatients, there was no difference in VBR between the bipolars and the unipolars. The possible correlates of VBR were further investigated in the outpatient sample, in whom more detailed longitudinal information on the course of the illness and its treatment was available. The length of time since the onset of the psychiatric disorder, number of admissions, number of episodes, and duration of hospitalisation were all significantly greater in the manic-depressives than in the neurotics ($P < 0.01$), although the two groups did not differ in percentage of time psychiatrically ill since onset. Ten manic-depressives and six neurotics had suffered definable physical illness since they became psychiatrically unwell (NSD). (Table I) The only illness which occrured in more than two patients was hypothyroidism; the other outpatients had had their thyroid function checked and were known to be euthyroid. VBRs of hypothyroid and euthyroid outpatients were compared, with age as a co-variate, and it was found that the mean VBR of the hypothyroid patients (12.8) was significantly greater ($P < 0.025$) than that of the euthyroid

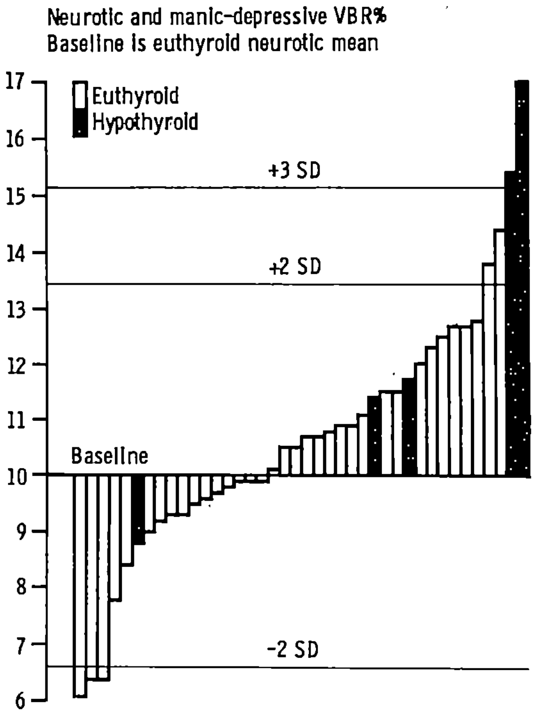

FIG 1 VBRs of hypothyroid and euthyroid outpatients in relation to euthyroid neurotic mean.

TABLE II

Description of the thyroid status of the hypothyroid patients

Case (group	*Age*	*Nature of hypothyroidism and basis of diagnosis*	*Time of diagnosis of hypothyroidism in relation to scan*	*Biochemically euthyroid at scan*	*Good control of thyroid function at routine checks since diagnosis*	*Last demonstration of euthyroid state before diagnosis of hypothyroidism made*	*Antibodies*
MM (M/D)	54	Low serum thyroxine & T4/T3 uptake index; elevated TSH	7 m before	+	+	1 y before	negative
MR (M/D)	61	Partial thyroid ectomy for removal of thyroglossal cyst, placed on thyroxine 1–2 y later (1967); stopped thyroxine June, 1976; euthyroid Dec, 1976; hypothyroidism diagnosed on basis of low serum thyroxine & T4/T3 uptake index, March, 1979	18 m before	+	+	2 yr 3 m before	+ve thyroid microsomal & parietal cell antibodies
PW (M/D)	63	Low serum thryoxine & T4/T3 uptake index; elevated TSH	2 y before	+	+	1 y before	thyroid micro somal strongly +ve
AF (N)	55	11 y before at another hospital notes unavailable	11 y before	+	+ (for 4 y at NPH)	unknown	not when seen at NPH
DL (N)	53	Low serum thyroxine & T4/T3 uptake index; elevated TSH	18 m later	?	+	3 y before	thyroid micro somal, mito chondrial, parietal cell all +ve

patients (10.4). The VBRs of the hypothyroid and euthyroid patients are illustrated in Figure 1.

The hypothyroid and euthyroid samples did not differ in terms of age, proportions of neurotics and manic-depressives, measurements relating to time and severity of illness, proportions of unipolar/bipolar in the manic-depressive sample, numbers of patients in whom alcohol abuse was a possibility, or years of prescription of tricyclics and other antidepressants, benzodiazepines and other anxiolytics, or neuroleptics. In contrast to the total sample, all the hypothyroid patients were female ($P<0.05$ Fishers Exact test), and the years of prescription of lithium were greater in the hypothyroid than in the euthyroid sample ($P<0.05$).

TABLE III

Correlations between years of drug treatment and VBR in euthyroid cases

Drug	*R*	*Probability*	*No of cases ever given drug*
Lithium	−0.08	NS	10
Tricyclics	0.42	$P<0.05$	26
Other anti-depressants	0.01	NS	8
Neuroleptics	0.09	NS	11
Benzodiazepines	0.15	NS	25
Other anxiolytics	0.28	NS	4

Since hypothyroidism is associated with lithium administration (Lindstedt *et al,* 1977; Lazarus *et al,* 1981), the relationship between VBR and past history of lithium treatment was re-examined. With age and sex taken into account, the VBRs of patients on lithium (mean 10.6) did not differ from those of patients who had not had the drug (mean 10.5). Moreover, three of the hypothyroid sample were manic-depressive and on lithium, but the other two were neurotic and were not. Correlations between VBR and years of lithium and other drug treatment were sought among the euthyroid sample (Table II). These results suggest that lithium treatment *per se* is not associated with ventricular enlargement. A significant positive association between ventricular size and years of administration of tricyclic antidepressants was demonstrated in the euthyroid sample ($r=0.42$; $P<0.05$). Of the 26 patients who had received tricyclics, 25 had had them for a total of between one and ten years, but the remaining patient had been on this medication continuously since the 1950s. If this patient were eliminated, there would be no significant relationship between VBR and years of tricyclic administration r = 0.17, N.S.). The Withers & Hinton test battery (1971) showed no difference between the hypothyroid and euthyroid samples (mean score euthyroid 86.8: mean score hypothyroid 90.8 NSD).

Discussion

Correlates of VBR were sought in this sample of manic-depressive and neurotic patients, but few were found. Among the outpatients, there was a significant association between hypothyroidism and greater VBR. Thyroid disease was more common than would be expected in the population in general (Tunbridge *et al*, 1977), but an association between affective illness and its treatment and hypothyroidism is well established. Lithium treatment is, of course, associated with the development of hypothyroidism, but it has been claimed that affective illness in itself is associated with an excessive frequency of impaired thyroid function (Editorial, 1977). The lack of association between VBR and lithium treatment and the fact that two of the hypothyroid group had never received this drug suggest that it is hypothyroidism, rather than lithium treatment, that is associated with increased lateral ventricular size.

The possibility that hypothyroidism may result in a dementing illness has long been known (Asher, 1949; Jellinek, 1962). In 56 cases of hypothyroidism with neurological features, Jellinek (1962) found that 18 had psychiatric disturbance, and of these six were left with persisting dementia after thyroid treatment; however, in the study of Tonks (1964) only one of the five hypothyroid patients who showed an organic picture did not respond to thyroid treatment. The CT appearances of dementia resulting from hypothyroidism have not been described, but a degree of cerebral atrophy has been demonstrated with pneumoencephalography (Jellinek, 1962). The patients in the present study, however, showed no evidence of impaired cognitive function. Furthermore, in four of the five hypothyroid cases, there is evidence that the condition did not remain undetected and untreated for many years, and in all five there is evidence of good control of thyroid function. This suggests that even where diagnosis has been reasonably prompt, treatment has been reasonably satisfactory, and there is no evidence of cognitive impairment, hypothyroidism may be associated with central nervous system changes leading to lateral ventricular enlargement.

While schizophrenia was the first functional psychotic illness to be investigated with the CT scan (Johnstone *et al*, 1976), and it is in this condition that abnormalities have most frequently been reported, lateral ventricular enlargement has also been demonstrated in affectively ill patients (Rieder *et al*, 1983), among long-term benzodiazepine users (Lader *et al*, 1984), and as a phenomenon which may be reversible in association with alcoholism (Carlen *et al*, 1978) and anorexia nervosa (Heinz *et al*, 1977). The clinical correlates of ventricular enlargment in schizophrenia are by no means clear-cut, although they are unrelated to treatment (Owens *et al*, 1985), but in so far as they have been demonstrated, are of deterioration and defect. The development of such features is often used as a validating criterion for the diagnosis of schizophrenia and as one of the main points of separation between schizophrenic and affective psychoses (for review see Johnstone *et al*, 1985). It has been hypothesised that the cell loss presumed to underlie ventricular enlargement in schizophrenia may be the basis of the irreversibility of the schizophrenic defect state (Crow, 1980). If ventricular enlargement were demonstrated to be directly associated with affective illness—a disorder characterised by its reversible nature—this concept would be weakened. The present study indicates that hypothyroidism, a disorder associated with affective illness and/or its treatment, is a correlate of ventricular enlargement. Because of the association between affective illness, lithium treatment, and hypothyroidism, it is probable that some of the samples of affectively ill patients in whom ventricular enlargement has previously been demonstrated have included hypothyroid patients, although it is perhaps least likely to have been prominent in the study of Nasrallah *et al* (1982), which concerned relatively young manic men. While it is clear that schizophrenia, even in its most severe and chronic forms, need not be associated with ventricular enlargement, and that there is nothing specific about the ventricular enlargement that is sometimes seen in this illness, the present findings suggest that in affective disorder, ventricular changes may be attributable to a factor (hypothyroidism) not directly related to the disease process. No such factor has been demonstrated in studies of schizophrenia, in some cases of which increased VBR appears to be an intrinsic feature. The thyroid status of patients in CT studies of the brain is rarely reported, although in the original CT scan of schizophrenic patients at Northwick Park (Johnstone *et al*, 1976), all patients were shown to be biochemically euthyroid. It is thus unlikely that hypothyroidism is a determinant of increased ventricular size in schizophrenia, or indeed psychotic illness in general.

The present study is small, and the association between hypothyroidism and increased ventricular size was unexpected. This finding requires further exploration of its relevance to thyroid disease and affective illness, and to the management of both disorders.

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*Eve C. Johnstone, MD, FRCP, FRCPsych, *Member of Scientific Staff and Honorary Consultant Psychiatrist, Clinical Research Centre, Watford Road, Harrow, Middlesex HA1 3UJ.*

D. G. C. Owens, MRCP, MRCPsych, *Member of Scientific Staff and Honorary Consultant Psychiatrist, Clinical Research Centre.*

T. J. Crow, PhD, FRCP, FRCPsych, *Head of Division and Honorary Consultant Psychiatrist, Clinical Research Centre.*

N. Colter, BSc. *Research Officer, Clinical Research Centre.*

Claire A. Lawton, BA, MRCPsych. *Registrar in Psychiatry, Division of Psychiatry, Clinical Research Centre.*

R. Jagoe, BA. *Member of Scientific Staff, Division of Computing and Statistics, Clinical Research, Centre.*

L. Kreel, FRCP, FRCR. *Consultant Radiologist, Department of Radiology, Newham District General Hospital, London, E13.*

*Correspondence

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Brief Reports

Anniversary Reactions

E. B. RENVOIZE and J. JAIN

Recent bereavement is associated with increased psychological and somatic morbidity among the survivors (Parkes, 1975), but the long-term effects are less well documented. One late sequel of bereavement is the "anniversary reaction", and although the term implies a specific disease entity, it actually refers to a heterogeneous group of psychiatric and physical disorders which have in common the fact that they are precipitated in susceptible individuals by the anniversary of the death of a significant person, often many years after the bereavement. Anniversary reactions have also been described in relation to other periodicities such as specific time of day, day of the month, season of the year, festivals, birthdays, and holidays (Pollock, 1971).

Freud was aware of the powerful effect which anniversaries can exert on the mind. In his description of Fraulein Elisabeth von R. (1895); he wrote: "This lady celebrated annual festivals of remembrance at the period of her various catastrophies, and on these occasions her vivid visual reproduction and expressions of feeling kept to the date precisely". Anniversary reactions have since been reported in association with various psychotic and neurotic disorders (e.g. Hilgard & Newman, 1959; Mintz, 1971; Cavenar *et al*, 1976; Cavenar *et al*, 1977). Adults may be particularly vulnerable to psychiatric illness when they reach the age at which a parent died, and also when their own child reaches the age at which they themselves experienced the death of a parent in childhood (Hilgard & Newman, 1961). Sibling death in childhood may also lead to anniversary reactions in children (Cain *et al*, 1964) and in adults (Hilgard, 1969).

Suicide may be a fatal outcome of anniversary reactions: Zilboorg (1937) reported the case of a young woman who died by jumping out of a 14th storey window on Good Friday, on the 14th anniversary of her mother's death. Hilgard (1969) also described the case of a lawyer who killed himself with poison the day after his son reached the age of 12. The day following the lawyer's own 12th birthday, his older brother with whom he had experienced intense sibling rivalry, died suddenly and unexpectedly.The lawyer had throughout his life harboured a deep sense of guilt about his brother's death and a conviction that like his brother, he too would have to step aside through death to give his son an opportunity to develop his full potential.

Anniversary reactions associated with physical symptoms such as chest pain, headache, back-pain, abdominal pain, obesity (Mintz, 1971; Fischer & Dlin, 1972; Cavenar & Spaulding, 1977; Cavenar *et al*, 1978; Miller, 1978), and relapse of ulcerative colitis (Berliner, 1938; Engel, 1955) have also been described. Although some somatic anniversary symptoms are undoubtedly conversion reactions, others are clearly organic in nature. For example in studies of emotional factors in coronary occlusion, Weiss *et al*, (1957) and Fischer *et al*, (1964) observed that in some of their patients coronary occlusions occurred on the anniversary of the death of a key but ambivalent figure. Also, Yazmajian (1982) reported the case of a woman who lactated as part of an anniversary reaction to the delivery of her still-born child.

Pollock (1970) and Mintz (1971) have suggested that anniversary reactions are manifestations of pathological mourning. A variety of experiences including guilt, anger, relief, anxiety, reactivation of old conflicts, helplessness, somatic symptoms, and the denial and absence of emotion can occur in normal mourning, and the intensification of any one of these may be enough for mourning to become pathological (Siggins, 1966). Among the factors identified by her as contributing to this process include the sudden and unexpected occurrence of death, the manner of death itself, a highly ambivalent relationship to the dead person, and low tolerance of pain and anxiety.

Pollock (1970) argues that an anniversary represents a time of unconscious psychic stress, which serves as an activator for the emergence of repressed conflict, reflecting fixation at the developmental stage reached by the individual at the time of loss; this in turn gives rise to symptoms which reflect the original trauma. He also emphasizes that "a predisposing set must exist for this activator to have an effect. The vulnerability, sensitivity and predisposition are in existence before the actual reaction occurs". Evidence in support of this hypothesis comes from Engel (1975), who carefully documented his own physical and psychological responses in relation to the sudden and unexpected death of his identical twin brother, and also as he approached and lived through his own 58th year, the age of his father at the time of his sudden death.

In the anniversary reaction, there is a close identification of the bereaved individual with the deceased person. This may result in the formation of somatic symptoms similar to those experienced by the dead person in his last illness, or a recurrence of the feelings the mourner himself or some third person such as a surviving parent was undergoing at the time of loss (Siggins, 1966). Krupp (1965) suggests that anniversary symptoms represent the unconscious gain of bringing back the lost loved one, and also self-punishment of the survivor for having wanted the other's death and for having survived it. Mintz (1971) explains anniversary phenomena by invoking the concept of repetition—compulsion in which trauma to the psyche is revived by the sense of time and the need for mastery through re-experience. Some anniversary symptoms may also be rooted in Chapman's (1959) nemesis feeling, when a patient is convinced that he is destined to follow in his life pattern the general outlines of some other person's life, usually to a tragic end.

Mintz (1971) distinguishes between two types of anniversary reaction, depending on the presence or absence of a conscious stimulus to which the individual responds. In one type, a conscious knowledge of an event such as a birthday or holiday (a "conscious time symbol") may create a current conflict, which is then associatively linked to a specific earlier repressed and unresolved conflict. The ensuing anniversary reaction is a reproduction of an adaptation to that conflict on a specific date. In the second type of anniversary reaction, there is no specific current conscious stimulus. The stimulus is unconscious, and the reproduction of the conflict requires the presence of the ego's unconscious sense of time which, intimately linked with death, responds to conflicts over death and separation.

Anniversary reactions are probably quite common in clinical practice. Although the immediate medical management may not be influenced, recognition of an anniversary reaction may have therapeutic implications. Exploration of the relationship between the patient and person whose anniversary of death has precipitated the illness may clarify the meaning of current behaviour for the clinician and allow the patient to gain insight into the nature of the anniversary conflict. A working through of this conflict may also speed the recovery of the patient from the current illness, and may be hoped to prevent future recurrence of these "secret anniversaries of the heart, when the full river of feeling overflows" (Longfellow).

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*E. B. Renvoize, MD, MRCPsych, *Consultant Psychiatrist, Bootham Park Hospital, York, YO3 7BY*

J. Jain, MD, MRCPsych, *Consultant Psychiatrist, Burnley General Hospital, Lancashire BB10 2PQ*

*Correspondence

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Folie à Deux in Identical Twins: Interaction of Nature and Nurture

ARTHUR LAZARUS

The French term folie à deux literally means "insanity of two." It denotes a syndrome "characterised by the transference of delusional ideas and/or abnormal behaviour from one person to one or more others who have been in close association with the primarily affected patient" (Gralnick, 1942). Also known as the "psychosis of association" and "shared paranoid disorder," folie à deux was first described by Lasègue and Falret in 1877. Prior to that date, the condition had been encountered but it was not formally recognised.

Relatively few accounts have significantly added to our appreciation of folie à deux since that of Lasègue and Falret. One notable exception is Gralnick's (1942) detailed review, which synthesises much of the significant controversy surrounding the definition and concept of folie à deux. Also noteworthy is Dewhurst and Todd's (1956) paper. They listed three criteria generally considered prerequisite to diagnosing folie à deux:

1) evidence that the partners have been intimately associated;

2) identical or near identical delusional themes; and

3) acceptance, support and sharing of each other's delusions.

Application of these criteria ensures that non-specific genetically based psychoses are not mistaken for bona fide cases of folie à deux. This formulation is especially relevant to the following case of folie à deux in identical twins.

Case Report

The patients, A and B, are black identical monozygotic twin males born in 1964. It is difficult to distinguish them by appearance or behaviour. They have been closely associated since birth, having always occupied the same bedroom and attended the same schools. When they were students they would often report together to the counsellor's office complaining that they were "sick," "suffering," or had a headache or upset stomach. In August 1979 A presented to hospital with bizarre behaviour, including auditory hallucinations and persecutory delusions. Fifteen months later B was admitted with paranoid delusions similar to A. Both believed they were continually being made to suffer. They were convinced that others were spreading rumours about their inferior intelligence and abilities. The twins believed they were "time travellers" engaged in interplanetary travel and that both had special powers to ward off evil spirits. They claimed to be black angels who were able to see beasts which were mixtures of human and animal forms. Usually A would make the observation and B would verify it. Neither brother had used alcohol or illicit drugs. Results of psychological testing (Rorschach, Bender-Gestalt, Draw-A-Person, WAIS-R) were remarkably similar. Each brother exhibited schizophrenic-like thought processes and evidence of borderline mental retardation (Full scale IQ: A = 67; B = 71).

Despite treatment with neuroleptic drugs in adequate dose and sufficient duration to treat schizophrenia, each has continued to manifest similar paranoid ideas. They seem to have little insight and concern regarding their extreme interdependence.

Discussion

Many authors have recognised the importance of

TABLE
Cases of folie à deux in identical twins reported in English literature

Author(s)	*Relationship*	*Age*	*Type of delusion**	*Hallucinations*
Lasègue & Falret (1877)	sisters	41	P	no
Gill (1883)	sisters	20	P,G	no
Savage (1883)	sisters	28	D	no
Parsons (1883)	sisters	19	?	no
Tuke (1888)	sisters	23	?	?
Peterson (1890)	sisters	40	P	no
Gordon (1925)	brothers	21	P	yes
Grover (1937)	brothers	20	P	yes
Gralnick (1942)	sisters	66	P	no
Craike & Slater (1945)	sisters	52	P	no
Adler & Magruder (1946)	sisters	26	D	yes
Oatman (1947)	brothers	26	P	yes
Rioux (1963)	sisters	29	P,G	no
Potash & Brunell (1974)	sisters	34	P	yes
Gagnon (1979)	sisters	21	P,D	no

*P = Persecutory; D = Depressive; G = Grandiose

genetic (Kallmann & Mickey, 1946; Scharfetter, 1972) and environmental (Soni & Rockley, 1974) factors in the aetiology of folie à deux. Yet few have commented specifically on this feature with respect to twins. Rioux (1963), reporting on twin sisters, stated: "It (folie à deux) is to be considered a psychosis which develops because of a faulty and peculiar association of persons, which transcends the twinship itself." Tuke (1888), on the other hand, believed that the "constitutions [of twins]. . . . .were so nearly identical, that the existing causes of insanity produced when operating on them, the same results."

In the present case, the contribution of genetic and environmental factors appears to be equal. Whereas the concordance rate for schizophrenia in identical monozygotic twins is about 50% (Kinney & Matthysse, 1978), equally impressive is their psychological similarity, parallel life experiences, and unique interpersonal relationship. Hence, even in the face of indisputable genetic loading, special psychodynamic and environmental forces seem to play just as important a role in producing a shared paranoid disorder in twins. The symbiotic aspect of the relationship and the similarity of delusions distinguishes folie à deux from other cases in which individuals are genetically predisposed to non-specific psychoses (Dewhurst & Todd, 1956).

Even though folie à deux is very rare (fewer than 300 cases have been published), its occurrence in identical twins is much less frequent. Gralnick recorded only nine such cases from a total of 103 which had been reported in the English language literature up to 1942. (An additional case appeared in the French literature and was reported by Lasègue and Falret in 1877). An extensive review of the literature subsequent to 1942 disclosed only six more cases (Craike & Slater, 1945; Adler & Magruder, 1946; Oatman, 1947; Rioux, 1963; Potash & Brunell, 1974; Gagnon, 1979). One case appears to be a diagnostic misnomer since the twins were reared apart and there was no association prior to the emergence of their similar paranoid delusions (Craike & Slater, 1945). Of the total 16 reported cases of folie à deux in identical twins, 12 involve twin sisters (see Table). This is consistent with Gralnick's (1942) observation in the general population that sister-sister combinations predominate in folie à deux.

Treatment of folie à deux usually entails separating the affected individuals (Lasègue & Falret, 1877). Thereafter, psychotherapy and chemotherapy may be required, especially if one or both partners suffers from any underlying functional psychosis (Enoch & Trethowan, 1979). Drucker and Shapiro (1982) have pointed out that separating psychotic twins may be traumatic and may cause further psychologic decompensation. In the absence of physical separation, cases of folie à deux in identical twins have been successfully treated with electroconvulsive therapy (Adler & Magruder, 1946), multiple conjoint psychotherapy (Potash & Brunell, 1974), and milieu therapy (Gagnon, 1979), but none of these methods have been tried in the present case.

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Arthur Lazarus, MD, *Instructor in Psychiatry, Temple University Health Sciences Centre, 3401 North Broad Street, Philadelphia, Pennsylvania, 19140, USA.*

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Normal Dexamethasone Suppression Test in Obsessive-Compulsive Disorder

W. MONTEIRO, I. M. MARKS, H. NOSHIRVANI and S. CHECKLEY

The dexamethasone test (DST) has been proposed as a "specific laboratory test for the diagnosis of melancholia" (Carroll *et al*, 1981). It is agreed that many depressed patients have abnormal DSTs and that in general, these abnormalities return to normal as the patient recovers from depression, but less agreed are the clinical characteristics of those depressed patients with dexamethasone resistance (abnormality). Although discrepant findings have been reported, it is in general the more "biological" categories of depression such as endogenous depression, bipolar depression, and delusional depression in which abnormal results have been reported (Checkley 1985; Carroll *et al*, 1981).

To be of diagnostic value, the DST must be more common in depression than in conditions with which depression can be confused; in this respect, it is unfortunate that dexamethasone resistance has been found in some, though not all studies of dementia and schizophrenia.

It may be that the DST is of greater value in the differentiation of depression from neurotic disorders. Normal DST results have been reported in patients meeting DSM III (1980), criteria for "panic disorder" and agoraphobia (Curtis *et al*, 1982; Lieberman *et al*, 1983; Sheehan *et al*, 1983). The distinction between depression and obsessive-compulsive disorders is of particular clinical significance.

Obsessive-compulsive symptoms are common in depression (Lewis, 1934; Gittleson, 1966; Kendall & Discipio 1970), as are depressive symptoms in obsessive-compulsive disorders (Marks *et al*, 1980; Lewis 1966: Rosenberg 1968; Goodwin *et al*, 1969). In addition, antidepressants are useful for obsessive-compulsive disorders (OCD) when anxious and depressed mood (dysphoria) is present (Marks 1983). If OCD and depression are independent, and if the DST is indeed a marker for depression, then OCD patients with normal mood should suppress normally, while those with "endogenous" depression should escape suppression. In one study, among 16 patients with OCDs, the DST was positive in six (37%), but five of the six had high Hamilton Depression scores (above 20), while the remaining patients had been recently depressed (Insel *et al*, 1982). Cottraux *et al*, (1984) found that 30% of 20 OCD patients had abnormal DSTs, and that these patients did not differ in their Hamilton Depression scores from those with a normal DST. Asberg (1983) found 50% of "escapers" in a sample of patients with obsession compulsive disorders.

Method

The sample. We report here the result of the DST in 61 patients with OCDs on DSM III Criteria. To qualify, patients should have had the problem for at least one year, be in the age range 18–59, have no history of psychosis, and agree to stop all previous psychotropic medication including benzodiazepines, beta blockers, and alcohol for at least three weeks before the test (benzodiazepine use may normalise plasma cortisol response to dexamethasone (Langer *et al*, 1979).

To clarify whether or not uncomplicated OCD is associated with an abnormal DST, we analysed such patients complicated by other factors known to produce such abnormality separately from cases without such complications. Examples of complications associated with an abnormal DST are major depression (two patients in our series), medical illness or alcoholism (two of our patients turned out to have cancer and one alcoholism) and current anorexia nervosa (AN) with low weight (Doerr *et al*, 1980; Gerner & Gwirtsman 1981); we had one such patient). We also had four patients with a *past* history of AN; our first patient to have unsuppressed DST had a clear past history of AN, present normal weight and eating habits, and absence of other factors known to produce this. We therefore decided to examine: (a) the frequency of a past history of AN in OCD and (b) the effect of such a history on the DST. We chose to analyse results of the latter patients together with those who had complications known to be associated with anormal DST.

Procedure

Dexamethasone test: Patients were asked to take two tablets of dexamethasone, i.e. 1 mg at 11.30 p.m. At 4.00 p.m. the following day, 10 mls of blood were drawn and placed in a heparinised tube. This was centrifuged for ten minutes and the plasma placed in a glass tube and frozen immediately.

Analysis of plasma cortisol: Plasma cortisol was analysed by a radioimmunoassay method using the Amerlex cortisol kit. According to Wood *et al*, (1983), this gives results which are comparable to those obtained by the CIS International method. Based on normative data obtained from the latter method, we adopted a cut-off of 138 n.mols/lit (5 mg/–dl) as the upper limit of a normal 4 pm post-dexamethazone cortisol value.

Measures

All clinical measures were made long before results of plasma or urine analysis became available.

a) *Compulsive checklist: 37 0–3 items (total score range 0–111):* a self-rated broadscan measure of rituals.
b) *Beck depression inventory* (BDI) (Beck *et al*, 1974): 13 items, range 0–39, self rated.
c) *Wakefield depression inventory* (Snaith *et al*, 1971): score range 0–45, self-rated.
d) *Hamilton depression scale* (Hamilton 1969) items 1–17, score range 0–52, assessor-rated.
e) *Demographic data:* past history—family history.
f) *Semi-structured depression interview* Schedule for affective disorders and schizophrenia (Spitzer *et al*, 1978).
g) *Urine test* for alcohol and psychotropic drugs.

Results

Clinical characteristics

Obsessive-compulsive scales: 61 patients were diagnosed as having severe obsessive-compulsive disorder on DSM 111 and ICD 9 criteria. They scored a mean of 35 (SD 21.4) on the compulsive checklist.

Depression scales: The patients were not depressed as a group, with normal mean scores of 14 (SD 7.1) on the BDI and of 9.5 (SD 6.0) on the Hamilton depression scale, but had raised Wakefield depression inventory scores—a mean of 24 (SD 6.8). On the Research diagnostic criteria (Spitzer *et al*, 1978) only two patients qualified for a definite diagnosis of major depression, four had possible major depression, and seven qualified for a diagnosis of minor depression. Correlations (Pearsons product-moment) were 0.80 for the Hamilton v Beck ($n = 61$), 0.79 for the Beck v Wakefield ($n = 50$) and 0.71 for the Hamilton v Wakefield ($n = 50$) (all $P < 0.001$). None of these scores correlated significantly with the plasma cortisol levels of the DST.

Patients' characteristics: Mean age was 32 (SD 9.9). The patients had been ill for an average of 12 (SD 8.8) years, and mean age of onset was 20 years. There were 30 men (11 married, 2 divorced) and 31 women (15 married, five divorced, three widowed). Of the 61 patients, 41 checked excessively, 39 washed excessively, and 40 ruminated excessively. Most had more than one of these problems. Only three patients had a family history of treated obsessive-compulsive illness, 12 of treated depression, and three of unspecified but treated psychiatric illness, six had close relatives with depression.

Other drugs: All patients were asked to abstain from drugs and alcohol for three weeks preceding the test. A urine test done at the time of the DST showed that our patients were free of psychotropic drugs and alcohol, except for three, who were on 75 mg, 100 mg, and 200 mg of tricyclic antidepressant per day.

Other pathology: Among our sample of 61 patients with obsessive-compulsive disorder, four had a past history of AN (of whom two also occasionally abused alcohol, although not at the time of the DST) and one was anorexic but much improved when seen. One patient abused alcohol, another was a permanent night worker and so had probable altered diurnal rhythm, and over the next six months two of the remaining patients were discovered to have cancer, requiring surgery. Two had definite major depression. This left 49 patients without any of these complications or definite major depression.

Dexamethasone suppression test

Forty-eight of our 50 uncomplicated cases of OCD suppressed cortisol normally.

Among the 11 remaining patients, two suppressed normally, and nine escaped suppression. Of the two patients with definite major depression, one suppressed normally and one escaped suppression. The four patients with a past history of AN escaped suppression; they were eating normally, and did not appear anorexic either at the time the DST was performed or over the next few months. The one with ongoing AN escaped suppression. Of the two patients who were discovered to have cancer in the following months, one suppressed normally (uterine cancer) and one escaped suppression (seminoma of testis). The patient who worked night-shifts escaped suppression, as did the patient with alcohol abuse.

After six months, the DST was repeated in 20 patients. The 15 who had previously suppressed normally remained suppressed, and five who were unsuppressed remained unsuppressed.

Discussion

Only two out of our 50 uncomplicated cases of OCD failed to suppress cortisol (4%), in marked contrast to 37% and 50% respectively of the obsessive similar patients of Insel *et al*, (1982) and of Asberg (1983), or the 50% rate usual in melancholia. Cottraux *et al*, (1984) found that 30% of 20 OCD cases had abnormal DSTs, and that these patients did not have different Hamilton depression scores from those with normal DST scores. Two factors may explain these differences: (1) the co-existence of depression and OCD in other samples, e.g. a mean of 17 on the 17-item Hamilton in Cottraux' sample, indicating moderate depression, compared to a mean score of 9.5 in our sample. Rabkin *et al*, (1983) found that 18% of even mildly to moderately depressed patients may escape suppression; and (2) the possibility that some patients in other series with higher rates of anormal DSTs had similar complications to some of ours, e.g. a past history of AN, which as we have found, is not uncommon in obsessive-compulsive disorder.

Reports of occasional abnormal DST in anxiety disorders (Williams *et al*, 1983, Sheenan *et al*, 1983) might be explained by the common association with such problems as varying degrees of depressed mood, alcohol abuse, or past history of AN. Among reports of uncomplicated agoraphobia with panic, all 17 patients of Curtis *et al*, (1982) and all ten patients of Lieberman *et al*, (1983) suppressed normally.

We examined depressed mood carefully in this sample, using a semi-structured interview and three depression scales. On two of the three measures of depression our sample showed normal mood. On the third, the Wakefield, high scores could be produced by anxiety as well as depression. Only two of our patients had a definite diagnosis of major depression, and very few had a family history of depression or of OCD. All except three of our sample had been free of psychotropic drugs for three weeks before the DST.

Most anorexics have a positive DST (Gerner & Gwirtsman 1981) that usually reverts to normal after feeding to 80% of their ideal body weight (Gwirstman & Gerner, 1981). Four of our patients (8%, or 16% of the females) had a history of *past* AN; unexpectedly, all these four escaped from suppression, in spite of apparent current normal weight and eating habits. This obviously needs to be investigated further, and has to be accounted for in further studies of the DST.

It would be of interest to present data on DST findings in future studies of OCD and of other diagnostic categories in a similar way. Some studies in which abnormal test results are reported in non-depressed patients make little or no reference to such associated conditions. Our data suggest that in the case of OCD, the DST is normal unless there are other complications associated with its abnormality.

In conclusion—patients with OCD had a normal DST unless they were complicated by alcoholism, depression, a history of anorexia nervosa, cancer, or a reversed diurnal rhythm. Of the female obsessive-compulsive patients, 16% had had AN.

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W. Monteiro, MRCPsych. *Research Worker and Senior Registrar.*

*I. M. Marks, MD., FRCPsych. *Professor of Experimental Psychopathology.*

H. Noshirvani, MRCPscyh. *Research Worker and Senior Registrar.*

S. Checkley, BM, MRCPsych. *Consultant Psychiatrist, Institute of Psychiatry and Maudsley Hospital, London SE5 8AF.*

*Correspondence

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Books Reconsidered

*The Discovery of the Asylum: David J. Rothman**

Professor Rothman's book made a profound impression on me when I first read it. More to the point, perhaps, was the impression it made on his peers. The American Historical Association awarded it the Albert J. Beveridge prize for the best English language book published in American History. It is a beautifully written account of an exciting and ultimately tragic episode in American history: the attempt to use the institution as a means of reforming bad habits and curing mental illness.

Some may think that this is already a well told tale: the high hopes of "moral treatment" followed by the disappointment and pessimism at the end of the century. Professor Rothman's account covers a much wider field, encompassing the care not only of the mentally ill but of the poor, the orphan and the criminal.

In post-colonial America a wind of change blew from the same quarter over all these groups. It came from Europe and the libertarian ideas of the Enlightenment. Its message was that punishment often brutalised; instead the individual should be reformed. In colonial times, gaols were small, casual places where deviants of all sorts were kept for a short time to await a rough and at times brutal justice. Before Independence there had been pressure for more humane legislation, but the Crown had disallowed it. In the post-colonial era, the nation's need to assert its independence added impetus to the movement for reform.

Reform of deviance and the cure of insanity could not really begin until their causes had been ascertained. This, however, was not a difficult task. The roots of the problem lay in faulty upbringing, bad company, and the structure and demands of society. These conclusions were based, not on guess work, but on the finding of careful inquiries. For instance, Prisoner No. 315:

> "A.N., born in Massachusetts; father was killed at Quebec when he was very young; family soon after scattered, and he was bound out to a farmer, with whom he lived till of age; was a wild, rude boy, and early addicted to some bad habits, drinking, swearing, etc."

The fact that he had committed forgery at the age of 55, after an apparently respectable life, did not alter the conclusion that the origins of his deviancy were laid down many years previously. Or, take another example:

> "Of the 156 inmates recently admitted to Pennsylvania's Eastern State Penitentiary, 14 had been orphaned by the age of 12, 36 were missing one parent or another soon thereafter, 143 had received no religious instruction, and 144 never attended Sabbath school. 'Such statistics' affirmed William Channing, one of the founders of the New York Prison Association, 'tell at a glance that early neglect was certainly in part, probably in great part, the cause of after crime'."

The same notions informed the cure of the insane, but with an extra emphasis on the temptations and strains afforded by a society whose aspirations were becoming limitless. Thus, Isaac Ray contended that youngsters contemplated life "not as a field of discipline and improvement, but a scene of inexhaustible opportunities for fulfilling hope and gratifying desire". Under this training, patience and perseverance "become distasteful to the mind which can breathe only an atmosphere of excitement... It reels under the first stroke of disappointment, turns upon itself... and thus it is that many a man becomes insane."

To find the origins of poverty in a country with limitless opportunities was a harder task. Surveys, however, indicated that, to some degree, and particularly in the case of the chronic poor, that the problem lay with the individual's own bad habits. In New York, in 1821, the Society for the Prevention of Pauperism announced that "the paupers of this city are, for the most part, depraved and vicious, and require support because they are so". Drinking was a particularly common vice. Significantly, taverns were much commoner in the precincts of the lower classes. But it was totally wrong and unfair to blame only the poor. Society set all sorts of traps and temptations. Did it not licence the taverns and permit the sale of liquor? The poor should be relieved, but also protected and removed from society to be reformed.

The same arguments applied, *a fortiori*, to children: orphans, runaways, those with poor or incompetent parents, and delinquents. What could be more important than to remove these unfortunates "from those baleful influences which inevitably tend to make them pests to society and ultimately the tenants of our prisons", and to provide them with

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*(1971) Boston: Little Brown. £14.00

"a healthy moral constitution, capable of resisting the assaults of temptations, and strong enough to keep the line of rectitude through the stormy and disturbing influences by which we are assailed".

Professor Rothman emphasises that this general move towards reform and asylum was by no means a response to an overwhelming public clamour to remove problematic people. It arose from philanthropic and humanitarian concern. The regimes applied in the asylums were based on the latest theories, some of which were keenly debated. For instance, the total isolation of each inmate practiced at Pennsylvania Penitentiary, thus avoiding the contagion of vice, competed with the more partial separation advocated at Auburn, New York. Both were places of pilgrimage for the new penologists both at home and from Europe, and both had their passionate advocates and denigrators. The regimes of the children's asylums followed closely the prescriptions of current manuals in child care.

For the insane, the first stage, too, was removal, and visitors were to be strictly limited and preferably banned for, said Isaac Ray "the patient might otherwise be as well at large as in the hospital for any good the latter may do him by way of seclusion". Within the asylum the emphasis was on orderliness and a predictable routine, regular occupation and non-restraint.

The gradual change in the character of the asylums during the ensuing 30 years is graphically described, with illustrations of their increasing size. The Boston Almshouse and Blackwells Island Penitentiary in New York, built in 1849, were already vast, brooding buildings. Of greater concern to us, perhaps, is the gradual change in the claims and attitudes of the staff and the public towards these institutions. By the 1860's "the asylums were admitting great numbers of chronic patients, the poor houses were taking in the aged and decrepit, penitentiary cells filled up with hardened criminals and even the reformatories received teenagers surprisingly advanced in a life of crime". To be sure, the staff protested both at their new clientele, and at their inadequate funding, but the shift from reform to custody was not accompanied by any great demand that the system be dismantled. "The promise of reform had built up the asylums, the functionalism of custody perpetuated them". In the case of the insane asylum, the change to chronic containment was soon accepted by staff and public alike. Indeed, it was recommended. For, in addition to the dangerous effects of the family on the patient, Isaac Ray warned of the reverse risks "that the poor sufferer cannot receive the ministry of near relatives without endangering the mental integrity of those who offer them".

It is easy at this distance to criticise the enthusiasm and naivety of the reformers, and what seems like their sanctimonious hypocrisy and paternalism. But they were men of their time, and our own current views may appear equally naive to our descendants in 100 years. To avoid repeating history we have to try to learn its lessons. Large institutions are comparatively recent arrivals on the psychiatric scene. Compared to other examples of the architectural expression of a faith—cathedrals for instance—they are very recent indeed. Their monumental size gives a misleading impression of permanence. Total solutions are always dangerous and often disastrous. "One cannot help but conclude this history", writes Professor Rothman, "with an acute nervousness about all social panaceas. Proposals that promise the most grandiose consequences often legitimate the most unsatisfactory developments".

Instead, surely, we require imaginative and varied contributions to what Karl Popper calls piecemeal social engineering. Reform is less exciting but more productive than revolution. Certainly there are moments when one wonders whether the "wheel of progress" is not even rotating on one spot but merely being rediscovered. 111 Denmark Hill, the Hospital Hostel at the Maudsley, and previously a private house, bears an uncanny resemblance to the building illustrated at the very beginning of Rothman's book—the New York Almshouse of 1735. "Built in the style of an ordinary residence, the almshouse followed, internally and externally, the organisation of the family". For a history of the 1980's it provides a promising first illustration. But the subsequent ones? *Absit omen.*

Post Script

Readers may be interested to know that Professor Rothman, who is, incidentally, a Professor of Social Medicine and of History at Columbia University, has written two further books on the subject: *Conscience and Convenience: the Asylum and its Alternatives in Progressive America*, (1980), describes how waves of progressive ideas broke helplessly on the inertia of asylums and other bureaucracies. The second, the *Willowbrook Wars*, (1984), written with his wife, a social worker, describes the judicial and other struggles concerned with the reform of a huge New York institution for the mentally handicapped.

J.L.T.B.

J. L. T. Birley, FRCP, FRCPsych, *Consultant Psychiatrist, Bethlem Royal and Maudsley Hospitals, Denmark Hill, London SE5 8AZ.*

British Journal of Psychiatry (1986), **148**, 332–344

Correspondence

Social Interventions in the Families of Schizophrenics

DEAR SIR,

The paper by Leff *et al* (*Journal*, June 1985, **146**, 594–600) is highly unsatisfactory. The number of patients is surely far too small for there to be any validity in the study, yet the conclusions seem to be widely quoted in the psychiatric literature. The design of the experiment was also poor. The patients had no standard drug treatments. Some had injections and others had tablets. The chemical state of those on depot injections varies throughout the period between injections, whereas for tablet takers the condition of the patient does not vacillate so much. The patient may be knocked out for a few days after his injection and towards the end of the period he may become less well due to shortage of medication. Skill in medicating patients would seem to be the first essential in preventing relapses of all schizophrenics. Often medication is not skilfully given and relapses result.

Another drawback to the study is that only one in each group was suffering from paranoid schizophrenia and the rest from nuclear schizophrenia. There are two points here. The families in which there is a paranoid patient would be likely to have suffered in a different way from those with a member suffering from nuclear schizophrenia. I would expect families with a paranoid schizophrenic member to be more emotionally upset when reporting on the behaviour of their ill one. They would be likely to show more high EE. Secondly, it is possible that there were others in some of the families who are genetically a bit high and without the help of medication they would not be able to change themselves. I heard one distraught mother say at a recent meeting "I am a high EE mother". Poor woman, I wonder if undue pressure was being put on her to change.

I think that the worst part of the study is perhaps the figures. 2/10 relapsed in the experimental group and 7/9 in the control –20%:78%, which the authors say is a highly significant difference. However, 3 of the 7 in the control group who relapsed were suicide attempts. They lived. Two of the experimental group actually committed suicide. They did not relapse, but they died. Their cases were thus far worse than the hospitalised attempts at suicide. If the two suicides are added to the two relapses in the experimental group, the differences between the two groups were not significantly different. This would seem to make the study of no worth, especially remembering the small numbers of people involved.

The authors also quite openly state that the high suicide rate (17%) amongst the control group might be attributed to their interventions. If they had been trying to help the young girl suicide to loosen the attachment to her mother it is quite possible that they did hasten her demise. Her mother was most probably the girl's main support and she needed her far more than she needed intervening psychiatrists.

Although the patients were randomly selected the much higher average age of the experimental group to the control (41:30) and the higher age of onset in the experimental group compared to the control (36:26) would be expected to affect the results. When the six experimental cases are cited it would appear that most of them were reasonably stabilised on drugs so that they were able to engage in interesting activities. The fact that they were mostly older was possibly related to the average late onset of their illness, which had enabled them to live pretty normal lives before onset. We are not given similar case histories for the controls.

Lastly, the very fact that the researchers did not repeat the EE assessment at the end of the 2 year study meant that they failed to do what they set out to do. They do not know if their interventions could in any way have been said to reduce high EE to low EE. The second suicide lived alone, so he had almost nil face to face contact and neither was he living with a high EE or a low EE relative. Face to face contact was reduced in the others due to their jobs etc. I doubt very much if reduced contact in these families played any part in the prevention of relapse.

GWYNNETH HEMMINGS

The Schizophrenia Association of Great Britain
International Schizophrenia Centre
Bryn Hyfryd, The Crescent
Bangor, Gwynedd LL57 2AG

Dr Leff and Colleagues Reply

DEAR SIR,

The methodological issues raised by Mrs Hemmings are either accommodated by the randomisation procedure we used to assign families to experimental or control groups, or have been given due consideration in our accounts of the 9 month and 2 year follow-ups. We sympathise with the aim of the Schizophrenia Association of Great Britain of identifying the biological basis of the illness, and eventually a cure. However, until that is achieved, it seems to us worthwhile exploring ways in which families can be helped to cope with this devastating illness. In fact, we were able to change the family environment in the desired direction in three-quarters of the families we tried to help. This resulted in a zero relapse rate at 9 months and a 14% relapse rate at 2 years, for those patients who remained on medication. Mrs Hemmings has chosen to concentrate on the minority of experimental families whom we were unsuccessful in helping. The patients in these families did very badly, a fact which causes us great concern. In the light of our accumulated experience of working with the families of schizophrenic patients, we now consider that the families in our trial would have benefited from more contact with us, rather than less, as suggested by Mrs Hemmings.

Regarding the generalisability of our findings, we have never claimed that our results can be applied to families other than those in which a schizophrenic patient is in high contact with a high EE relative. However, three other trials of family treatment have been published (reviewed by Leff, 1985) which cover a wide range of patients and families, each of which achieved benefits for the patients very similar to ours.

J. LEFF
R. BERKOWITZ

MRC Social Psychiatry Unit
Friern Hospital
London N11 3BP

L. KUIPERS

District Services Centre,
Maudsley Hospital
London SE5 8AF

D. STURGEON

University College London

Reference

LEFF, J. (1985) Family treatment of schizophrenia. In *Recent Advances in Clinical Psychiatry, Vol. 5* (ed. K. Granville-Grossman). Edinburgh: Churchill Livingstone.

Depression in General Practice

DEAR SIR,

Dr Sireling and his colleagues recently published two papers on Depression in General Practice to which we should like to respond (*Journal,* August 1985, **147**, 119–136). In them, different groups of "general practice depressives" are compared and contrasted with themselves and with a sample of psychiatric out-patients chosen for inclusion in an antidepressant drug trial. We believe their conclusion that GP depressives are "considerably less severe, with fewer depressive symptoms and shorter illnesses, as well as less primary and less endogenous" than psychiatric out-patients, is one forced upon them by the choice of their samples and by the problems they encountered with low patient recruitment.

To begin with, all patients who had recently received a prescription of antidepressants or had seen a psychiatrist were excluded from the study. We suggest that this strategy will have effectively "creamed off" many of the more severely depressed patients who might otherwise have legitimately been included under the rubric "general practice depression".

Thereafter three groups of "general practice depressives" were obtained. The first two consisted of patients who had been identified as depressed by the GPs, who had been newly prescribed antidepressants (group A) or any other forms of treatment (group B), and had thereafter been notified to the investigators. The decision of a GP to prescribe antidepressants or other treatment (including a simple follow up appointment) is not the same as a diagnosis of depressive illness. It is interesting therefore to note that 20% of the antidepressant group and 50% of the "other treatment" group failed on interview to receive a diagnosis of depressive disorder (major or minor) at all. Despite this, the authors make comparisons of severity between these psychiatric out-patients and the *entire* cohort of patients seen in groups A and B, not just those who had a diagnosis of depressive disorder.

The third group (group C.) of "missed major depressives" too may have been biased towards milder disorders and disorders of a certain kind because of the problems the authors experienced with low patient recruitment: 11% of age-eligible patients failed to complete the screening questionnaire (GHQ), and of those who scored above the threshold, 34% declined the subsequent diagnostic interview. We suggest that the authors will therefore have "lost" a significant number of depressed patients in their sample—especially those who are more severely ill, who are male, and who are somewhat atypical. In our own study of depressive disorder in primary care (Blacker & Clare, in preparation) we obtained a 97·5% GHQ completion rate and 93% interview response rate in a sample of just over 2300 patients. We found that those patients who were unwilling to complete a questionnaire or be interviewed, were highly likely to be suffering from some form of emotional distress (such as bereavement) or psychiatric disorder (typically alcoholism, major depression, and/or personality disorder). We also found a significant number of patients who had quite severe illnesses such as DSM-III melancholia. Sireling's depressives seem rather mild by comparison and we wonder therefore, since they had a good spread of practices, where the severe cases went? Evidence that Sireling and his colleagues have probably missed a substantial number of potential "cases" in their screening is shown by the low GHQ-positive score rate (24%) they obtained. Generally speaking most other studies report above-threshold rates on the GHQ somewhat in excess of this suggesting therefore that the 11% who declined to complete the questionnaire in the present study may well have been suffering from some form of psychological disturbance. In our sample of 2300 London general practice patients we found that 52% of patients scored above the threshold (4/5) on the GHQ!

This emphasises, we believe, the need for high patient-recruitment rates in epidemiological studies of this kind as well as the problems with interpreting data from studies in which these rates are low. That primary care depressives when taken *as a whole* should be found to be less severe than psychiatric service depressives is not perhaps surprising. One will always find this differential of severity in a health service where referred patients are "creamed off" from a relatively dilute pool of disorders in primary care and concentrated in psychiatric outpatients. The question remains whether those more elusive depressives who defy recognition by the GP, who decline to participate in research studies, who consult less frequently, or who belong to different areas of general practice (such as domiciliary consulters or those who "go to" repeat prescription) are suffering from disorders which might be described as severe and who might, despite this severity, defy referral to psychiatric services? The statistics on suicides, most of whom have been found to have consulted the GP shortly before death but few of whom are in contact with psychiatric services, are one indication that this "elusive" group may be substantial!

C. V. R. Blacker
A. W. Clare

St Bartholomew's Hospital
West Smithfield
London EC1A 7BE

Dr Sireling and Professor Paykel Reply

Dear Sir,

We are grateful for the opportunity of replying to the comments by Dr Blacker and Professor Clare. They clearly believe that general practice depression is more severe than we found it to be, but they have produced no evidence for their belief, and their methodological criticisms have little bearing on the question of severity. We will deal with their comments in turn.

They suggest that the exclusion of patients who had seen a psychiatrist or received antidepressants in the past three months would have "creamed off" many severely depressed, and that the approximately 10% of depressed patients whom general practitioners refer to psychiatrists cannot be legitimately regarded as "general practice depressives".

We would agree that the decision of the general practitioner to prescribe is not the same as a diagnosis of depressive illness: it is precisely because of the ambiguity of the word "illness" that we chose to adopt the operational definition "depressed enough to require treatment". This surely is legitimate "general practice depression". In the same way,. the psychiatric outpatients were all regarded as requiring antidepressant treatment—to distinguish between those who were and were not "ill" in either sample would be arbitary. If Blacker and Clare only regard as depressives those patients given a diagnosis of "depressive disorder" (on criteria developed by psychiatrists on the basis of condition seen in psychiatric patients), how would they label the large numbers of general practice patients depressed enough to require treatment, including antidepressants, but not meeting the formal criteria for "disorder"?

We would agree that the patient recruitment rate in our study was lower than we would have liked, but we had to strike a balance between consent and coercion in the surgeries, which may have led to an under-estimation of the frequency of missed depression. Blacker and Clare produce no evidence that the *severity* of cases, as opposed to their frequency, would be underestimated, particularly since all our cases had further to satisfy the Research Diagnostic Criteria for major depressions. As they have not yet published their study, it is impossible to comment on their methodology, but demographic and sampling differences may help explain the disparity between their positive GHQ rate of 52% and ours of 24%—most British studies of consecutive surgery attenders find a rate closer to ours than to theirs, for example, Goldberg and Blackwell (1970) report a rate of 32%, and Goldberg, Kay and Thompson (1976) a rate of 25%.

Finally, we look forward to reading Blacker and Clare's findings on general practice depression, and hope that the differences—as well as the similarities—between the studies will help elucidate the nature of these disorders.

L. I. Sireling
E. S. Paykel

Springfield Hospital
61 Gleburnie Road
London SW17 7DJ

Depression in School Phobia

Dear Sir,

We read the paper by Kolvin, Berney & Bhute (*Journal*, October 1984, **145**, 347–357) with interest and disagree with many of its conclusions which serve only to obfuscate the diagnostic precision of depression in childhood. The authors demonstrate circular reasoning when they conclude that their criteria are different from Weinberg's but similar to the RDC. We wish to point out that the Weinberg criteria are based on the RDC.

The key items that Kolvin and colleagues put forward account for 5 of the Weinberg criteria. We wonder what has happened to the others, in particular, concentration problems and childrens' school performance, as both these are important cognitive variables. In Brumback's paper (1977), depressed children did in fact, endorse 6 or 7 of the 10 Weinberg criteria and they also used a semi-structured closed-ended interview with good inter-rater reliability. There is no indication about those parameters by Kolvin and his colleagues.

Unfortunately, this paper by Kolvin *et al* has some serious problems with regard to its aims. The first is quite reasonable, to identify subgroups in a population of children with school phobia using clinical and statistical methods. However, to identify a depressive subtype and to then develop a criterion for depression in the absence of a control group is totally invalid. As the authors observed all of these children studied may represent a spectrum of severity of depressive illness and not distinct diagnostic groups.

Finally, to conclude that depression has a multifactoral origin obscures the finding that many of these children have an underlying substrate of right cerebral dysfunction and that the dependent variable in 80% of the cases is a positive family history as reviewed by Brumback *et al*, 1980. Further nosology will be dependent upon the discovery of state-independent biological markers and state-dependent biological correlates.

Warren Weinberg
Graham Emslie

Children's Medical Center of Dallas
1935 Amelia Street
Dallas, Texas 75235

Chris Wilkes

University of Texas Health Science Center at Dallas
5323 Harry Hines Blvd.
Dallas, Texas 75235

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Brumback, R. A., Stanton, R. D. & Wilson, H. (1980) Neuropsychological study of children during and after remission of an endogenous depressive episode. *Perceptual Motor Skills*, **50**, 1163–1167.

Dear Sir,

Kolvin *et al* (*Journal*, October 1984 **145**, 347–357) addressed the issue of depression in school refusal. But liberal use of (1) χ^2 procedures and (2) principal components analysis probably inflated the discriminant validity of depression measures and resulted in spurious association of these with other variables studied.

(1) In testing the discriminatory efficacy of five compound depressive indices, Kolvin *et al* sought that point which maximally discriminated depressed and non-depressed subjects. This "best cut" procedure works to exploit chance data fluctuation (Cronbach, 1949). Implicit in the approach are S-1 (where S = number of scores in a range) comparisons, though only the most advantageous is reported. The result is to increase Type I and per experiment error rates. For example, the chance probability of Kolvin *et al* finding a significant difference on the 21-item Total Global Depression Score is approximately 21-1 x .05 = 1.00; on the 15-item Global Score it is about 14-1 x .05 = .65; on the "11 items-cut-of 5+" it is around 11-1 x .05 = .50.

Also the "best cut" approach probably inflated artifactually the discriminant efficacy (rates of sensitivity and specificity) of the variables in question. This is serious, given the authors' own admission that most of the indices were not highly sensitive in any case. A preferable approach would have been to make the cuts on theoretical grounds *a priori*, or to use the median split.

(2) In two principal component analyses, Kolvin *et al* met none of the prerequisites ensuring valid factor extraction (Wade, 1978).

(a) A recommended *minimum* ratio of subjects to variables is 5:1. As the ratio moves towards unity, factor analytic results become increasingly meaningless. Kolvin *et al* performed analyses with approximately 2 and 3.6 subjects per variable.

(b) The recommended *minimum* number of subjects for any factor analysis is 100. Kolvin *et al* used 50 participants in one analysis, 47 in the other.

(c) Correlation matrices should be tested for psychometric adequacy prior to factoring. Kolvin *et al* reported no data on matrix adequacy.

(d) Determination of number of interpretable factors is problematic. In their second analysis, Kolvin *et al.* interpreted two factors without reporting criteria for doing so.

(e) Given that factor analysis imposes as well as extracts structure, some measure of replicability is necessary. Kolvin *et al* might wisely have subjected the data to an alternative factor extraction technique and tested for congruence.

(f) Kolvin and coleagues' criterion factor loading of .2 is extremely low. Explaining only $.2^2 = 4\%$ of the variance, it is substantively meagre and statistically vulnerable to chance data fluctation. Moreover, in the text itself, Kolvin *et al* interpreted variables with loadings as low as $-.13$ (Unreality index) and $-.15$ (Recent obsessionality).

Many of these shortcomings are serious even in isolation. Combined, they severely undermine conclusions drawn by Kolvin *et al.*

LESLIE ATKINSON

Whitby Psychiatric Hospital
Whitby, Ontario L1N 5S9
Canada

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Folate Deficiency in Dementia

DEAR SIR,

The report by Hancock and colleagues (*Journal*, October, 1985, **147**, 404–407) is a further confirmation of widespread malnutrition in the elderly mentally ill including those in institutions (Thomas *et al*, 1982) and those in the community (Shaw *et al*, 1984).

Their findings of the common occurrence of deficiencies in vitamins C, B_2 and B_6 prompt us to report the results of a survey of folate levels in patients with dementia.

Seventeen male and 28 female demented patients who were electively admitted into the dementia research bed at St George's Hospital were studied. Their ages ranged between 67 and 96 years (mean 78.7 years). These patients were admitted for one week mostly from the community to carry out a large battery of clinical and biological investigations including cognitive (orientation test), behavioural rating scales and 14 sub-tests of cortical function. Biological investigations included haematology and biochemistry profile. Diagnosis of dementia was confirmed by computerised tomography. Seven male (41%) and nine female patients (32%) were found to have folate deficiency (serum folate <2.5 ng/ml). There was no association between folate deficiency and classification of dementia and the degree of cognitive and cortical dysfunction. Folate deficient patients however were significantly older than those with normal folate levels $P<0.03$. There was a significant association between folate deficiency and increased erythrocyte sedimentation rate (ESR) and increased thyroxine levels (T4). Interestingly, only one folate-deficient patient had increased mean corpuscular volume (MCV). There was no association between folate deficiency and the presence of physical illness and any concurrent prescribed medication.

We have previously reported the common occurrence of folate deficiency (serum and red blood cell folate) in drug-free depressive and lithium treated patients (Abou-Saleh, 1985). More recently Coppen and his colleagues (to be published) have explored the usefulness of daily physiological supplements of folate (200 μg) in the management of 75 patients on prophylactic lithium and in the context of a double-blind placebo-controlled trial. During the trial, patients with the highest plasma folate concentrations showed a significant reduction in their affective morbidity and patients who had their plasma folate increased to 13 ng/ml or above had a 40% reduction in their affective morbidity.

The implications of these results for nutritional hypotheses for the psychoses have been discussed (Abou-Saleh & Coppen, 1986). It is conceivable that supplements of folic acid and other vitamins should enhance the recovery of the elderly mentally ill both in institutions and in the community.

M. T. ABOU-SALEH
E. SPALDING
J. KELLETT

St George's Hospital
Cranmer Terrace, Tooting,
London SW17 0RE

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DEAR SIR,

The article by Renvoize *et al* (*Journal*, August 1985, **147**, 204–205) stressed the importance and usefulness of comprehensive physical investigations in the assessment of demented patients. However, in their findings they reported that folate deficiency was present in 44.8% of their patients. This was based on serum folate assay, and it is noteworthy that despite this high prevalence of "folate deficiency" as they call it, no reference is made to this finding in their discussion. There are two important points to be made here. First of all, it is probable that the elderly as a population tend to have a lower serum folate (Caird, 1973; Fox *et al*, 1975) and therefore the reference range used should be stated. But more importantly, it is now established that a low serum folate is not diagnosis of "folate deficiency". It has been stressed (Chanarin, 1983) that a low serum folate may better be interpreted as negative folate balance, possibly dietary in origin, but for the diagnosis of folate deficiency red blood cell folate level is required. It is therefore more appropriate to perform red blood-cell folate assay in the investigation of demented patients.

GREGORY O'BRIEN
ANDREW CLARK

Fleming Memorial Hospital
Great North Road
Newcastle upon Tyne NE2 3AX

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Research on the Value of Psychotherapy

DEAR SIR,

The controversy over the value of psychotherapy (*Journal*, May 1985, **146**, 555–557) has raged for some time, and will no doubt continue to do so. I believe that an important aspect of the problem involved in evaluating psychotherapy deserves greater attention, viz. the differences between the methodologies of the natural (explanatory) and human (interpretive) sciences.

I believe that it is important to recognize a particular way in which the two sciences differ, because it underlies a great deal of the controversy. The difference consists in the fact that only in the natural sciences does the *theoretical* possibility exist that a crucial experiment can be undertaken to settle a question with absolute finality. Thus in physics it is possible to contemplate an experiment, in which all appropriate variables are controlled, all measures error free, and all outcomes ultimately predictable. Physicists of course, do not believe this is possible *in reality* and seem content to operate in a universe in which the creator does indeed throw dice. However, the ultimate experiment can be *imagined* and, therefore, used as a basis for theorizing.

In the human sciences on the other hand, it is very difficult to imagine an ultimate error free, totally manipulable and predictable experimental exercise, even if only because of the ethical implications. But when the object of interest is a social group, a historical event, or a sequence of individual behaviours in the field, replicability is a concept which cannot apply in the ordinary sense.

It is this sticking point that I believe needs to be elucidated in terms of current medical and social utilities if the "value of psychotherapy" controversy is to advance beyond polemics.

It might help matters if the supporters and decriers of the value of psychotherapy each described the design of a study whose outcome would satisfy them that the issue had been satisfactorily settled. Are there any who would take up this challenge?

I. PILOWSKY

Royal Adelaide Hospital
Adelaide, South Australia 5001

Psychotherapy and Placebo

DEAR SIR,

Professor Eysenck (*Journal*, May 1985, **146**, 556–557) points out that the inclusion of placebo controls is a necessary condition for the validity of psychotherapy research, and the logic of this appears inescapable.

However, there are problems about the use of the concept "placebo" in psychotherapy research. For since the effects of placebo are psychological and the treatment in question (i.e. psychotherapy) is also "psychological" then we are simply comparing like with like—psychological with psychological. In this situation we are faced with two alternatives; either we can say, as J. D. Frank (1961) used to do, that the placebo effect is *only one* of "a number of features common to all types of psychotherapy which probably contribute more to their efficacy than the characteristics that differentiate them"; or we can say, as Frank now does (Frank, 1983) that the placebo *is* psychotherapy. On the former view we are then faced with the problem of disentangling "placebo" from "psychotherapy" effects. In 1961 Frank attributed the effects of placebo to the "alleviation of anxiety and arousal of hope." Yet a decade later his pupil I. D. Yalom (1970) listed "instillation of hope" as one of the operative mechanisms in the process of group psychotherapy. And what of, say, suggestion? A hypnotherapist would regard this as the "specific" ingredient of his treatment, whereas a psycho-analyst or a behaviour therapist would see it as a "non-specific" or "placebo" ingredient of theirs. It is clear that the categorisation of such mechanisms into one or other pigeon-hole is purely arbitrary, and depends upon the point of view of the therapist concerned.

If, on the other hand, we adopt the latter alternative and say with Frank that the placebo *is* psychotherapy (and I agree with this) then a number of problems are solved. In the first place the need to distinguish "placebo" from "psychotherapy" is removed. Secondly, the behaviour therapist can henceforward use patients treated with general "non-specific" psychotherapy as his "placebo controls" against his supposedly specific mode of treatment. This is, of course, what Sloane *et al* (1975) did ten years ago though they did not then regard their "psychotherapy" patients as "placebo controls" against his supposedly specific mode of treatment. Thirdly, if, as seems likely, those especially efficacious factors which are common to all forms of psychotherapy are centred in the personal relationship between therapist and patient (or between person and person), then we can equate "psychotherapy effects" with "therapeutic relationship" effects. Furthermore, if "placebos" produce beneficial psychological effects (and the presumption that they do provides the need to control for them), and if, as Prioleau *et al* (1983) have recently concluded, psychotherapy effects are approximately "equivalent" to placebo effects then we are left with the approximate equation: placebo = beneficial psychological effects = psychotherapy = therapeutic relationship, and therefore placebo = therapeutic relationship.

It may be that, because "placebos" have unfortunate associations with inert pills, we tend to underestimate their value. On this view, rather than deploring the fact that psychotherapy is *no better than* placebo as Eysenck (1983) does, we should on the contrary welcome the evidence that the effects of therapeutic relationships are *at least equivalent* to those of placebos—and the former are infinitely more meaningful than inert pills. Nor need psychotherapy be unduly expensive in departments such as that at St Mary Abbots where the total psychotherapeutic effort is pooled amongst the various members of the multidisciplinary team.

MICHAEL DE MOWBRAY

St Mary Abbots Hospital
Kensington, London W8

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Irritability

DEAR SIR,

Snaith and Taylor (*Journal*, August 1978, **147**, 127–136) raise some very important issues as to psychiatric research on irritability. Their tentative conclusions are that "outwardly expressed irritability is an independent mood disorder and not merely one which is symptomatic of states of depression or anxiety" and that its finding in post-natal mood disorder indicates a state rather than a personality trait.

An often overlooked issue in self-rating scales is the psychometric distinction between the measurement of a trait (a long standing disposition) and distress (a temporary and changeable state) (Kellner, 1971). The responses to items in a personality inventory should be stable over time, but responses to items in a distress scale should change over time and measure changes in the clinical state of a patient (Kellner, 1971). Many scales consist of a mixture of trait and state variables. An unfortunately common example of this confusion is the Minnesota Multiphasic Personality Inventory, unreliable both in terms of personality configuration (because of lack of stability over time) and state determination (because variability over time is not treated as a source of error) (Gleser, 1975). Also the measurement of irritability is hindered by difficulties in discriminating its trait and state dimensions. Results may largely depend on the type of inventory employed. Readily available indications come from the relationship of hostility and irritability to depression, reviewed in detail elsewhere (Fava *et al,* 1982; Fava *et al,* in press). Although the evidence as to a direct correlation between hostility and depressed mood is conflicting—and also Snaith and Taylor observed a lack of correlation—several reliable studies suggest that hostility in depressed patients decreases with improvement in mood disturbances. Interestingly, in a study (Fava *et al,* 1982) that was performed in Italy, it was found that depressives displayed more hostility yet not less friendliness than a normal control group. These data were replicated in a more recent work in the United States (Fava *et al,* in press), where hostility decreased in melancholic patients after treatment with amitriptyline to such an extent that—upon recovery—there were no significant differences between patients and controls, whereas such differences were striking during the illness. In both studies the results were obtained by using the hostility and friendliness scales of the Symptom Questionnaire (SQ), a self-rating scale of psychological distress (Kellner, in press). The hostility-irritability scale is based on factor analyses and consists of 17 items such as "angry", "feeling of hate" and "hostile", and the six item scale for friendliness was constructed from antonyms with items such as "feeling friendly" or "feeling kind to people". In several published studies the SQ was found to fulfil the psychometric requirements for a pure state or distress measurement: the hostility scale significantly decreases upon pharmacological treatment and not with placebo or upon completion of prenatal diagnostic procedures, and discriminates between patients and controls (Kellner, in press). Its test-retest correlation in normals is very high ($r=0{\cdot}93$) (Fava *et al,* in press), indicating a high consistency of response in subjects whose state remains unchanged.

Each individual may have his own irritability threshold. Anger and hostility may be a personality trait, as discussed by Snaith and Taylor. In some cases, however, affective disturbances such as depression may lower this threshold and irritable mood may ensue. Behavioural scientists ought to be aware of the psychometric distinction between state and trait and of the limitations of their psychological instruments when studying the clinical aspects of irritability and hostility.

GIOVANNI A. FAVA

Dipartimento di Psicologia
University of Bologna
I-40127 Bologna, Italy

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Plasma Amino Acids, Downs Syndrome and Dementia

DEAR SIR,

Patients suffering from senile dementia (Alzheimer's disease), have been shown to exhibit a reduction in the ratios of both tryptophan and tyrosine to the sums of the larger neutral amino acids (Shaw *et al,* 1982) competing with them for transport across the blood brain barrier (Lajtha, 1974). This is likely to alter the relative amounts of these amino acids supplied to brain tissue, and thus to change the pattern of synthesis of proteins in the central nervous system.

Identification of patients undergoing the changes of early dementia of Alzheimer type is an uncertain exercise, and instead of this we have studied the nutritional status of individuals with Downs syndrome, a condition which is almost invariably associated with the pathological changes of Alzheimers disease (Burger & Vogel, 1973) if sometimes not the cognitive deficits (Hewitt *et al,* 1985).

There were significant differences between the plasma amino acid patterns of a group of 19 patients with Downs syndrome compared with an age and sex matched group of individuals with subnormality from other causes. Most of the latter had had brain damage at birth, and any with inborn errors of metabolism or who were receiving anticonvulsant drugs were excluded.

The findings in Down's syndrome included significantly higher plasma concentrations of cystine (1.6 ± 0.2 v 0.8 ± 0.2, mean $\pm$S.E.M., uMol.L^{-1}, $P<0.002$), leucine (125 ± 4 v 112 ± 4, $P<0.02$), phenylalanine (56 ± 2 v 51 ± 2, $P<0.05$) and isoleucine (71 ± 2 v 64 ± 2, $P<0.05$) and the ratios of leucine, of phenylalanine and of isoleucine to the sum of the 11 other large neutral amino acids also were raised ($P<0.02$, <0.001 and <0.001 respectively).

In view of the mode of entry of amino acids into the brain, these data point to a possible source of abnormality in the central nervous system in young adults with Downs syndrome in terms of availability of substrate for protein synthesis.

It is suggested that this aspect of metabolism may merit further investigation both in Downs syndrome and in senile dementia itself.

This research was completed from a Welsh Office grant.

SARAH E. WATKINS
MICHAEL A. CLIFFORD
SIMON F. TIDMARSH
VALERIE E. COWIE
DAVID M. SHAW*

University of Wales
College of Medicine
Whitchurch Hospital
Whitchurch, Cardiff CF4 7XB

ERIC AH-SING
JOHN W. T. DICKERSON

Division of Nutrition and Food Science
University of Surrey
Guildford GU2 5XH

**External Scientific Staff of MRC*

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Mental Health Act and Medical Treatment Without Consent

DEAR SIR,

I thought your readers may be interested in an aspect of the new Mental Health Act which appears extremely illogical.

I have currently on my ward a lady suffering from a severe chronic intractable depression with extreme retardation so that communication with her is impossible. Because of her inability to give valid consent I have already had to have three second opinions from the Mental Health Commission. At the time of the renewal of her Section I was informed by the Commission that if I wished to use any further treatment I would have to get yet a further fourth second opinion. A few days ago this lady appeared to be in pain and appeared to hold her leg in an abnormal posture. Her hip was x-rayed and this revealed a fracture of the acetabulum. My orthopaedic colleagues informed me that operative intervention was unnecessary and that she needed to be treated with analgesia alone as she did appear to be in such discomfort. As this lady was unable to give valid consent and as analgesia could not be constituted as a life saving procedure, I contacted the Commission to provide a second opinion to allow me to prescribe it. I was informed by the Commission that for medical treatment such as this I did not require their opinion even though valid consent could not be obtained. I was told that if in my clinical judgement as a doctor analgesia was necessary then I could prescribe it.

It seems strange to me that I am allowed to make clinical judgements about my patients in non-psychiatric areas and prescribe medication for them, but I am not allowed to do this in the one field I would consider myself to have some expertise in, namely the management of her depression. Also I wonder if I would be allowed to use antidepressants in this patient without a second opinion, on the basis that there is now considerable evidence that antidepressants have an analgesic effect!

C. J. THOMAS

Leicester General Hospital
Gwendolen Road
Leicester LE5 4PW

Transcultural Psychiatry

DEAR SIR,

I am delighted that Dr de Pauw (*Journal*, November 1985, **147**, 585–586) thinks I am passionate. Passionate or not, however, I am not responsible for the vagaries of the *Comprehensive Textbook of Psychiatry* (although if it says two different things in two different places that seems rather comprehensive).

The issue appears to be this: what reliance can be placed on the reports of colonial psychiatrists as to the actual occurrence of certain traditional behaviours variously termed the "culture-bound syndromes"? I am not entirely clear about de Pauw's point: the argument for *windigo* is in dispute, so the problem is solved by suggesting there is an "ethnopharmacological basis" for the *zombi*, implying the colonial psychiatrist got it right every time.

I was merely saying we have to "examine more closely" the so-called culture-bound syndromes (*Journal*, July 1985, **147**, 93) and pointed out evidence for and against "voodoo death". This is nothing to do with *zombis*, *vodun* or even Haiti. It is one of the terms bequeathed to us by European psychiatrists in Africa and Australia, and is perhaps more properly termed *psychogenic death*.

As to Haiti, Douyon and Wade Davis (1983) do not claim that tetrodotoxin causes people to be "raised in a comatose trance from the grave and forced to toil as a slave". Wade Davis' evidence is that intraperitoneal injections of local poisons into rats produce "catalepsy", and similar symptoms have been noted in diguatera and tetrodotoxin poisoning (as found in the consumption of the Japanese delicacy *Fuga pardalis*).

The term *zombi* (and the cognate *jumbi* as it is called in rural Trinidad where I carried out my fieldwork in traditional medicine) has at different times had a variety of meanings: god (*power, orisha*), possessed initiate, soul or body, twin, skin disease, mildew and mushroom, let alone reanimated corpse (Thompson 1958, Deren 1970). My own informants offered related ambiguous and binary notions including lesbian (*zami*). *Zombi* is probably derived from Amerindiam *zemi* (twin soul) and is an indigenous psychological term, a rich, complex and subtle web of explanations of personal identity, selfhood, autonomy, action, causality and power. Mircea Eliade has gone so far as to say the term refers to mystical power in general, "the sacred". Interestingly, given the intensive fieldwork in remote areas of Haiti by numerous social anthropologists previously eg Métraux 1959), none came across the mysterious slave corpse beloved of the European imagination.

Apart from questions of scholarship and sensationalism, it may be relevant to emphasise again the dangers of scientism: reducing social patterns and belief to a single unitary biological cause, its "basis" as de Pauw terms it. Social meanings are ascribed to the phenomena of the natural world, whether they are stars, sexes or the dead. Mars (1947) found that one claimed *zombi* had neurosyphilis.

ROLAND LITTLEWOOD

All Saints Hospital
Lodge Road
Birmingham B18 5SD

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Phobic Neuroses in India: A Cross-Cultural Comparison

DEAR SIR,

We read with interest Drs. Raguram and Bhide's account of phobic neuroses in India (*Journal*, November 1985, 147, 557–560). While commenting on the lack of Indian studies specifically on this subject, they fail to mention an earlier report by us (Chambers *et al*, 1980) on phobic neuroses from the same institute. Apart from a clinical analysis of 39 phobic subjects seen during the first three years (1976–1979) of the eight years spanning Raguram and Bhide's study, we had carried out a cross-cultural Indo-British comparison of phobic neuroses.

The Indian part of our study was a similar retrospective case record survey of 39 patients (31 male and 8 female) diagnosed as having phobic neuroses (ICD-9 criteria) at the National Institute of Mental Health and Neurosciences (NIMHANS), India. The British part of the study involved analysis of case records of a group of 30 similarly diagnosed phobic patients at the Maudsley Hospital, London, UK. The Maudsley comparison group was drawn randomly from a series of 268 phobic patients treated at this hospital between 1972–1976, and matched for age and sex with the Indian group. One of the investigators (J.C.) analysed the case records in both hospitals.

We found that males (79%) predominated in the Indian group as compared to the British group (21%) confirming Raguram and Bhide's finding of a male preponderance in the Indian group. The median ages of presentation, duration of symptoms, social class and marital status did not significantly differ between the two groups.

Thirty-six percent of the Indian sample were graduates as compared to 11% of the British sample ($P<0.001$) suggesting that education promotes help-seeking behaviour for phobic patients in the Indian context.

The British sample contained significantly more patients with agoraphobia (Indian group: 27.5%; British group: 60%, $P<0.05$) and social phobias

(Indian group: 7.5%; British group: 35.5%, $P<0.05$) while phobias for sudden death (Indian group: 30%; British group: 10%, $P<0.05$) were more frequent in the Indian group. Associated somatic symptoms were significantly more frequent in the Indian sample, in keeping with earlier observations of the predominance of somatisation in non-western cultures (Carstairs & Kapur, 1976). Precipitating psychosocial stressors were more frequent in the Indian group (57.5%) as compared to the British group (40%; $P<0.05$). Family history of phobic illness was significantly less frequent in the Indian group (2.5%) as compared to the British group (9%; $P<0.05$).

Clearly, the clinical patterns of phobic neuroses in western and non-western clinic populations are not essentially similar as Drs Raguram and Bhide appear to conclude. Our data indicate important differences even after careful matching of the two groups. While these differences may indeed be due to a variety of psychosocial factors, more field studies are needed before venturing fanciful culture-based explorations.

M. S. Keshavan
V. K. Yeragani
J. Chambers

Lafayette Clinic
951 E. Lafayette
Detroit, Michigan 48207

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Neuroleptic Malignant Syndrome and Lethal Catatonia

Dear Sir,

In their review of the neuroleptic malignant syndrome (*Journal,* January 1986, **148,** 47–51) Abbott and Loizou correctly point out that it is clinically identical to Stauder's lethal catatonia; however, in common with previous writers on this subject they do not suggest how the two conditions may be distinguished. Lethal catatonia has been recognised for over a century as a rare and dramatic cause of sudden death in mental patients, but in recent decades this diagnosis has suffered a curious eclipse. As described by the clinicians of the pre-neuroleptic era it typically presented with a prodromal phase of personality change, hyperactivity, affective disturbance, delusions, hallucinations, confusion and catatonia. Since the introduction of neuroleptic drugs in the 1950s, patients presenting with such florid psychotic symptoms will have received a major tranquillizer as a matter of course, and any subsequent hyperpyrexia may well have been attributed to the drug rather than the original disorder.

Is it then possible that all cases of neuroleptic malignant syndrome are in fact nothing more than the old lethal catatonia in spurious association with new and commonly-used drugs? The existing literature is not very helpful on this question: examination of published cases of neuroleptic malignant syndrome shows that many closely resemble the classic clinical picture of lethal catatonia (for example, the case described by Abbot and Loizou), but the uneven quality of description limits the conclusions that may be drawn by such comparisons (Peele & Von Loetzen 1973). Taken alone, however, these case reports cannot be regarded as adequate evidence for a separate neuroleptic-related condition. More convincing in this respect are descriptions of the syndrome in non-psychotic cases (Burke *et al,* 1981); cases where clinical course has been related to the kinetics of the implicated drug (Allan & White, 1972); and relapses of the condition following re-exposure to neuroleptics (Coons *et al,* 1982). Reports of typical cases in association with other dopamine-depleting drugs and with the withdrawal of dopamine enhancers such as levodopa also support the existence of a disorder secondary to iatrogenic disturbance of central dopaminergic transmission. However, it remains likely that the 'neuroleptic malignant syndrome' as we currently perceive it is a hybrid of this iatrogenic disorder and mis-diagnosed lethal catatonia.

If this clinical syndrome is indeed due to a disorder of dopaminergic function, then it is of some interest that one form of the disorder appears to have existed long before the introduction of major tranquillizers. In follow-up studies of the survivors of lethal catatonia there is a variable but persistant association with subsequent functional psychosis, usually described as schizophrenia (Arnold & Stepan, 1952). If the idiopathic form of this syndrome is associated with an increased risk of future schizophreniform psychosis, and the iatrogenic form with exposure to dopamine-blocking drugs, then the pre-neuroleptic accounts of lethal catatonia may represent important historical evidence in support of the dopaminergic theory of schizophrenia. This is an intriguing possibility and it deserves further study. However, it will first be necessary for us to rediscover lethal catatonia, and to develop criteria for distinguishing the idiopathic from the iatrogenic.

James Lindesay

UMDS (Guy's Campus)
London Bridge, London SE1 9RT

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Lithium and Piroxicam

Dear Sir,

Walbridge and Bazire (*Journal*, August 1985, **147**, 206–207) report an important interaction between lithium carbonate and piroxicam. In their discussion they seem to overlook the possibility of lithium toxicity having been precipitated by piroxicam further compromising the patient's already deteriorated renal function (creatinine clearance rate 51 and 55 ml/min on two occasions).

The consequences of prostaglandin inhibition by a non-steroidal anti-inflammatory drug (NSAID), such as piroxicam, on renal function in healthy subjects is controversial (Gullner *et al*, 1980). It is clear, however, that renal function is most likely to be adversely affected by a NSAID if it is already compromised (Sellars & Wilkinson, 1983). Prostaglandins become progressively more active with deteriorating renal failure (Calin, 1983). Renal prostaglandins (notably PGE2) are potent vasodilators of renal circulation. In experimental models of renal ischaemic stress, prostaglandin inhibition results in enhanced renal ischaemia since vasoconstriction is unopposed (Henrich, 1983).

The lithium toxicity may therefore have resulted from a sudden impairment of renal lithium excretion, mediated by prostaglandin inhibition by piroxicam.

R. K. Shelley

St Vincents Hospital
Elm Park
Dublin 4

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Schizophrenia with Good and Poor Outcome

Dear Sir,

The studies by Kolakowska and her colleagues (*Journal*, March, 1985, **146**, 229–246 and April 1985, **146**, 348–357) illustrate the difficulty of obtaining longitudinal information from a cross-sectional study. The authors attempted to relate CT scans, cognitive impairment and neurological soft signs to outcome of schizophrenia, but did not carry out these investigations on initial presentation; in most cases these examinations appear to have been done at or near the end of the outcome period. The authors found that enlarged ventricles and cognitive impairment were associated with unfavourable outcome, and went on to suggest that "organic deficit may contribute to an unfavourable outcome". This ignores the possibility that some of the abnormalities found may have been at least in part consequent upon poor outcome of factors associated with it rather than predictors of it.

The study is weakened by the high rate of attrition; only 59 out of 118 patients satisfying their inclusion criteria actually participated in the study. The authors are aware of this problem and state that "the sample cannot be considered as representative of the population from which it was drawn". This does not appear to have deterred them from making sweeping generalisations about possible sub-types of schizophrenia.

In our opinion, the demonstration that the ratio of plasma drug concentrations to drug dose does not differ between the various outcome or response groups is not proof enough to eliminate all likelihood of pharmacological tolerance in the patients receiving fluphenazine or fluphenthixol who responded unsatisfactorily to these drugs. Information about the tubero-infundibular-dopaminergic axis obtained from plasma prolactin levels cannot be extrapolated to other regions of the brain such as the limbic or cortical areas (Thorner & Evans, 1984). It also leaves unanswered the question of plasma levels of psychoactive metabolites, and also the possibility of pharmacodynamic tolerance.

Although we admire the industry of the authors, we are not convinced that the design of their study allowed them to do more than confirm a number of already known facts; e.g. that the prognosis is better in schizoaffective patients and worse in those with poor premorbid social adjustment who present early.

V. L. NIMGAONKAR
ROBIN M. MURRAY

Institute of Psychiatry
De Crespigny Park
London SE5 8AF

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Lorazepam Dependence and Chronic Psychosis

DEAR SIR,

Drs Fraser and Ingram report a nine-year psychosis in a Glasgow college student who became paranoid, withdrawn, neglected, deluded and possibly hallucinated, which they attribute to lorazepam from his G.P. (*Journal,* August 1985, **147**, 211). Benzodiazepines are the psychotropic medication most widely prescribed in general practice. That they can produce a classical picture of schizophrenia would surely be a most important discovery if substantiated.

However, another explanation is available. The college student recovered immediately after receiving about 120 mg of haloperidol in a fortnight. The fact that he then remained well for 6 months without medication would not be unusual in schizophrenia, particularly if the intervention had reduced his exposure to criticism and expressed emotion at home. The lorazepam may have been irrelevant.

In view of the importance of the issue they have raised, perhaps Dr. Fraser and colleagues could report follow-up on this case after, say, 2 years?

A. C. CARR

Institute of Psychiatry
De Crespigny Park
Denmark Hill, London SE5 8AF

Hypomania Following Cognitive Therapy

DEAR SIR,

We read with interest the report of the development of hypomania following cognitive therapy (*Journal,* January 1986, **148**, 103–104. However, we feel that there is a more parsimonious explanation of this event. This case appears typical of a bipolar affective disorder developing in middle life. The use of cognitive therapy is purely coincidental and there are no more grounds for attributing an aetiological role to this than to her filling in of numerous questionnaires. Extrapolation from a single case remains perilous and this hazard is not reduced when the authors outnumber the patient 'four to one' or by the inclusion of a graph.

A. M. HUGHES
J. P. MCKANE

Gartnavel Hospital
Glasgow

Misprint of the Year

DEAR SIR,

In Gellner's *The Psychoanalytic Movement* (St Albans: Paladin, 1985), the only reference to Freud's daughter calls her Anna Fraud (page 188). What kind of a slip is this?

ANDREW C. SMITH

Greenwich District Hospital
Vanbrugh Hill
London SE10 9HE

CORRECTION

In the INDEX TO VOLUME 147, July-December 1985, page 4, Dupuytren's contraceptive should read Dupuytren's contracture.

British Journal of Psychiatry (1986), **148,** 345–357

Book Reviews

Psychiatry, Human Rights and the Law. Edited by Martin Roth and Robert Bluglass. Cambridge: Cambridge University Press. 1985. Pp. 241. £27.50.

This collection of 16 contributions, derived from a 1983 conference at Trinity College, Cambridge, includes commentaries on British, American, German, Danish and Italian forensic psychiatry, as well as more theoretical chapters on values and policies (Margaret Sommerville), human rights and mental health (Larry Gostin) and dangerousness (Jean Floud). The British contributions, particularly those by Roth, Gunn and Hamilton, describe a somewhat sad state of affairs. The psychiatrically disturbed, if they are obstreperous or chronically disordered no longer get a fair deal. Nurses in open door NHS hospitals resist the admission of difficult-to-manage offender patients. Health policy no longer envisages mental hospitals as asylums for the mentally disabled, but rather as centres for short-term treatment. Unfortunately, the 'community care' that should have replaced them has so far been ineffective in keeping the chronically disordered out of trouble or preventing them from gravitating to prisons.

The need for facilities intermediate between the open door, through which anyone may wander on impulse, and the fortress-like special hospitals, has long been recognised and was urged by the Butler Committee over a decade ago. The arrival of medium secure units has been long delayed, it is doubtful if they will be enough to fill the need, and in any event they do not cater for the long-term sick.

Ideologically inspired deinstitutionalisation has had dramatically bad effects in some countries. Professor Stone notes (p. 10) that in the United States "50 to 75% of the homeless are chronic psychiatric patients—the deinstitutionalised." Tightening up of American legal procedures for civil commitment, with insistence on a criterion of dangerousness, has prevented many grossly disturbed patients from having the treatment they need unless and until they break out in some act of violence. According to Professor Sarteschi, deinstitutionalisation in Italy has diverted patients to geriatric nursing homes ill-equipped to deal with them and left others sleeping out on parks and railway stations. Some 30,000 families of the severely and chronically ill have formed associations to promote facilities to help them.

The use of psychiatry to produce explanations to excuse criminal behaviour is analysed by Professor Walker. He points out that pleas are often accepted that are mere possibility explanations, such as the presence of delusions or a schizophrenic illness, which make it more likely that an offender might behave in the way he did, but do not make the behaviour inevitable or even probable. Recognising this, he suggests that the concepts of diminished responsibility is more realistic than restrictively defined insanity. In England it is limited to murder, but it could be usefully extended to all crime and be used as a bar to imprisonment, thereby encouraging hospital commitment for the disordered.

D. J. West, *Emeritus Professor of Clinical Criminology Institute of Criminology, Cambridge*

Psychotherapy in the Third Reich: The Göring Institute. By Geoffrey Cocks. New York: Oxford University Press. 1985. Pp 326. £27.50.

In his heroic biography, *Sigmund Freud: Life and Work* (Vol. 111), Ernest Jones adroitly draws a picture in broad outline of the Nazi regime in Germany, undoubtedly the most obscene chapter in the history of mankind, and one in which, as a direct result, German psychiatry reached its nadir. What in effect Professor Cocks does in this book is to offer to his readers a full-scale portrait of these interdependent events. It will surprise no-one to learn that what emerges is disfigured by a welter of obnoxious warts.

Psychotherapy in any form was an anathema to the Nàzi ideologues, whilst psychoanalysis was regarded quite literally as a poison, a Jewish "poisoning of the soul". By the end of May, 1933, not long after Hitler had stormed to power, Freud's works together with other psycho-analytical books, were being publicly burned in the quadrangles of German universities. These Jewish analysts who had seen the writing on the wall had already begun to leave Germany mainly for America and some few for England: and by 1934 the majority had gone. It is important to remember, in the context of this particular exodus, that in Germany at that time, psychoanalysis was as inseparable from its Jewish practitioners as the Prince of Denmark is from Hamlet.

Nevertheless, it is perhaps an index of the innate strength of the psychotherapeutic movement in Germany immediately before and during the Hitler era that, despite the disastrous depredations it suffered, it managed to survive. It may not have done so at all except for the coincidence that one of the chief architects of National Socialism, Hermann Göring, Hitler's deputy, happened to be a cousin of Dr Matthuis Heinrich Göring, himself a Nazi and one of such dedication as to style himself "Reichsführer" and to parade himself before his professional colleagues in his SA uniform. Thanks to the patronage and protection of his infamous cousin, Dr Göring was able to set up an institute for psychotherapy in Berlin which was to be directed by him and which was to bear his name. The price he exacted from his associates at the institute was in itself an outrage: they were all, he commanded, to make a thorough study of Hitler's *Mein Kampf*, and on the philosophy therein contained they were to base their work.

For his pen-picture of Dr Göring, Professor Cocks dips his pen in vitriol. He portrays him as "of modest mien and accomplishment" who "owed his meteoric rise to professional prominence in 1933 not to his abilities but to his name. He did serve as an effective protector of his incipient profession, but as a psychotherapist he could not begin to rival these illustrious predecessors, many Jews and some not, whose place he took and whose careers he helped the Nazis destroy and whose reputations he helped them besmirch".

The constraints under which the Göring Institute worked, or was purported to work, made a mockery of accepted psychotherapeutic practice. An additional factor which must have added substantially to the charade was the blank refusal of the Nazi hierarchy to admit that neurosis is an illness. This obtuseness increased as the military situation deteriorated to a point where neurotic incapacity was deemed to be attributable to lack of moral fibre, a weakness to be dealt with by a firing squad or a hanging party rather than by a psychotherapist.

In April 1945 the Institute was raised to the ground in the allied air-attacks on Berlin, and Dr Göring himself was ignominiously taken prisoner by the Russians, and in July 1945 was to die of typhus in a detention camp. The violent destruction of Dr Göring and his Institute by fire and pestilence is mightily symbolic, and provides a final curtain of which, ironically perhaps, Richard Wagner himself would have approved.

The question remains: did this sordid story need to be told? The answer is undoubtedly "yes". We are indeed, deeply indebted to Professor Cocks for this book. It is a work of splendid scholarship, well researched, well written and beautifully produced. There is no attempt at a whitewash: the villains of the piece—there are no heroes—are portrayed in their true diabolical colours. More importantly, implicit in the terrible tragedy portrayed, is the grim reminder that the ghost of Hitler still stalks the world. C. G. Jung, whose attitude to the events in Germany in the early 1930's was, to say the least, ambivalent, seems by 1936 to have become disenchanted with Hitler and with National Socialism. In an essay entitled "Wotan" he writes: "The impressive thing about the German phenomenon is that one man, who is obviously 'possessed' has infected a whole nation to such an extent that everything is set in motion and has started rolling on its course to perdition".

We have been warned.

HENRY R. ROLLIN, *Emeritus Consultant Psychiatrist, Horton Hospital, Surrey*

Advances in Cognitive-Behavioural Research and Therapy. Volume 4. Edited by Philip C. Kendall. Orlando, Florida: Academic Press. 1985. Pp. 339. £45.50, $59.00.

This is the fourth volume in a successful series of books on developments in cognitive-behavioural research. It is a specialist publication, most pertinent to those working in the complex area of overlap between cognition, emotion and behaviour. Many of the contributions, however, have a speculative flavour which sets this series apart from the usual collection of dry, comprehensive reviews of esoteric areas.

Johnson's paper on the origin of memories is really concerned with experimental research pertinent to the process by which perceived and self-generated events are discriminated and confused in memory, the process of 'reality monitoring'. As in much cognitive work some of the conclusions are trite, (e.g. externally derived memories have more sensory attributes) but some of the experiments are ingenious (e.g. good visual imagers find it more difficult to differentiate between things shown to them and things they imaged on instruction than did poor imagers). She traces the clinical implications of a memory system that contains both external, stimulus-based events and internal events such as reflections and fantasies.

Constance Hammer's article is more traditional and contains a useful review of the current status of both Beck's and Seligman's models. She attempts to marry these with a socially orientated model but the evidence is not as yet forthcoming.

Dodge presents a summary of his work on attributional bias in aggressive children (aggressive children making more hostile attributions). He presents a set of hypothesized mechanisms (e.g. perceptual readiness) but these fall short of what would be required to disambiguate the status of such biases in a causal account of aggression.

The chapter by Lerner *et al* elaborates the findings of the New York longitudinal study concerning the importance of a 'good fit' between the child and its social context.

The most useful chapter is the one by Bradley and Kay which systematically traces the role of cognitive theory through a number of areas of behavioural medicine. Meimeyer's chapter brings repertory grids into cognitive behavioural theory and is remarkable for citing British construct theory research in an American publication.

On the whole the book is an interesting one, particularly the articles by Johnson and Bradley and Kay. Only one of the articles falls victim to the most prevalent affliction of cognitive theory, impenetrable jargon disguising the unspeakably obvious. Cacioppo *et al's* chapter on 'The elaboration likelihood model of persuasion' (i.e. that psychology undergraduates vary in how much they think about what is said to them), is a spectacular cavalcade of social psychological jargon (upcoming discrepant communications, anticipatory counterargumentations, the conservation of cognitive resources etc.) which is a resounding success in persuasion. Unfortunately the 'upcoming attitudinal stimulus' is that cognitive social psychology is entirely without redeeming scientific or social importance.

Despite the jargon and its enormous conceptual problems cognitive theory has come to dominate psychological approaches within psychiatry as in other applied fields. This book contains a fairly representative sample of sophisticated explorations within this framework. It is too specialist to provide a general introduction to the approach but those working in one of the problem areas covered by the book would do well to consult the pertinent chapters to obtain a flavour of the cognitive-behavioural view.

PETER FONAGY, *Lecturer in Psychology,*
University College London

Psychiatry: The State of the Art. Vol. I. Clinical Psychopathology, Nomenclature and Classification. Edited by P. Pichot, P. Berner, R. Wolf and K. Thau. New York: Plenum. 1985. Pp. 1122. $125.00.

This is the first volume of a mammoth undertaking, presenting the contributions to the Seventh World Congress of Psychiatry in Vienna in 1983. There are seven more volumes to follow. This one concentrates on the classification of psychiatric diseases and disorders. It wrestles with the difficulty of bringing sense and order into a field that lacks basic units comparable to the elements of modern chemistry or the species of modern biology. Once such basic units were established in the 18th century, successful classifications were possible. But psychiatry still has to struggle with polymorph complexes for which no basic units yet exist. It therefore has to rely on the classificatory and regularly revised efforts of expert committees whose decisions do not command general acceptance as many of the contributions to this volume testify. Foremost in the field are two nosological classifications: the ninth revision of the WHO *International Classification of Diseases* (ICD-9) and the third revision of the American Psychiatric Association's Diagnostic and Statistical Manual (DSM-III). There are in addition several research-directed diagnostic interview and rating schedules of which the best known is the Present State Examination (PSE) in its ninth edition which has been translated into more than 20 languages. But there is also the system of the German-Swiss Association for the Methodology and Documentation in Psychiatry (AMDP) in its second version (which has been translated into eleven languages including English), the French List of Integrated Criteria for the Evaluation of Taxonomy (LICET), the Viennese concept of endogenomorphic axial syndromes—to mention but a few which receive special attention in this volume. Several of such diagnostic systems can be combined in the so-called 'polydiagnostic' approach which aims to improve the comparability of research results, though it leaves out too many patients to be of great help to clinicians.

All these efforts run up against the variable interpretation of words and the established nosological customs in different countries. To give just one example: French contributors remarked that 'the French position of diagnosis and classification are, on the whole, viewed as unique and impossible to understand outside France'. They point out that the meaning of 'paranoid' changes from country to country, even from textbook to textbook in the same country; also that the DSM-III characterisation of the term is irreconcilable with that of ICD-9 and they are both different from Scandinavian and French usages. Different theoretical biases militate against semantic uniformities. French clinicians, for instance, adhering to psychoanalytical concepts, regard the various forms of anxiety disorders as one neurosis. DSM-III, on the other hand, while claiming to be non-theoretical in approach, divides anxiety disorders into three categories in accordance with the behavioural and biological theories held by the members of the relevant advisory committee which included Marks, Gelder, Saslow and D. F. Klein.

There are also chapters on therapeutic research, depression in schizophrenics, delusional misidentification syndromes (Capgras, Fregoli, etc), self-destructive behaviour, the psychopathology of artistic expression—to give just a few instances. There is obviously much grinding of old axes, but since many of the axes are Continental and overseas in origin, they have the tang of novelty for English readers. Some contributions are unfortunately marred by awkward translations into English. This hampers understanding and may even completely foil it, when the all too common printing errors play their additional havoc.

F. KRÄUPL TAYLOR, *Emeritus Physician, Bethlem Royal and Maudsley Hospitals, London*

Psychiatry: The State of the Art. Vol. 3. Pharmacopsychiatry. Edited by P. Pichot, P. Berner, R. Wolf and K. Thau. New York: Plenum. 1985. Pp 860. $87.50.

This is the third volume emanating from the VIIth World Congress of Psychiatry held in Vienna in 1983. The book consists of a large number of camera-ready copies of papers presented by speakers at the Congress and the results are predictable. My criticisms of Volume 3 are exactly the same as those made by Dr Trimble of Volume 2 in the October issue of the *Journal* (**147,** 457). Most papers that are presented at congresses have been published before in more readable and authoritative form and the only advantage of congress material is in synthesising and comparing developments in different subjects. *"The State of the Art"* is a cliché that is creeping into many scientific publications nowadays. I am not sure whether this indicates that it is independent of science but it certainly describes a state which is ephemeral. Publication of congress material therefore has to be quick for it to be of any value and it is astonishing that the publishers have taken so long to bind the pages that have already been submitted in publishable form at the congress.

The pharmacopsychiatry discussed in the book is a one sided business and only those who are interested in the therapeutic effects of buspropion, trazodone, pirlindole, carbamazepine and the benzamides, or problems with lithium therapy are likely to derive much interest from the book. As most of these could already have contributed anyway the market looks very small indeed. No individual is going to purchase this volume and libraries should beware unless they have an obsessional desire to collect.

PETER TYRER, *Consultant Psychiatrist, Mapperley Hospital, Nottingham*

Psychiatry: The State of the Art. Vol 4. Psychotherapy and Psychosomatic Medicine. Edited by P. Pichot, P. Berner, R. Wolf and K. Thau. New York: Plenum. 1985. Pp 533. $65.00.

Psychotherapy and Psychosomatic Medicine is the fourth of eight volumes reporting the Proceedings of the VIIth World Congress of Psychiatry, held in Vienna in 1983. The psychotherapy section contains papers on a wide range of psychotherapies and the application of these therapies in different settings; the range of papers in the section on psychosomatic medicine is equally wide, with papers in the section on psychosomatic pathology, eating disorders, liason psychiatry, and the future of psychosomatic medicine.

Some of the papers in this volume are excellent. For example, Schindler's discussion of the risks of short-term psychotherapy is superb. But others are hardly "state of the art". For example, Salem's paper on working with the family proposes as a novel idea what many units in this country have been doing for years. Likewise Battegay's paper on the different methods of group psychotherapy compares unfavourably with discussions of the same subject in introductory textbooks written four or five years earlier.

In between these two extremes are many papers of variable quality, clarity and interest, and with differing claims to the title "state of the art".

The book is very expensive (an unscrupulous person could photocopy it for considerably less than half the retail price!). The expense might have been justified if the book had come out very soon after the conference, and if it had been well printed. In fact it is already more than two years out of date, and contains almost as many different type-settings as papers. I would agree with the reviewer of Volume 2 (*Journal*, October, 1985, **147,** 457) that the better research papers would by now have appeared in journals, and that the majority of the review articles are not sufficiently comprehensive to stand alone.

The book (and presumably the whole series) undoubtedly reflect the state of the VIIth World

Congress. For this reason the series is of considerable historical interest, and it is desirable to have some record which can be studied by congress organisers in the near future, and by students of the history of psychiatry in the more distant future. But the state of the congress is clearly not the same as the state of the art of psychiatry. I therefore cannot recommend this book to the individual buyer, and do not think that the average institutional library should spend £750.00 to acquire the series.

MARK BERELOWITZ, *Senior Registrar in Child Psychiatry, Maudsley Hospital, London*

Understanding Human Behaviour in Health and Illness. Third Edition. Edited by Richard C. Simons. London: Williams & Wilkins. 1985. Pp 822. £26.00.

This book which has evolved from the human behaviour course at the University of Colorado, aims to provide students with an understanding of psychology and psychopathology. In the introductory section there is an account of psychological factors in medical illness and an exploration of the doctor-patient relationship and mind-body relationships. Particularly useful chapters consider the psychology of pain and the understanding and management of "difficult patients".

In the second section there is a comprehensive account of psychological development throughout life. The reader is introduced to psychodynamic concepts in chapters of unusual clarity. There are also descriptions of sexual physiology and the treatment of sexual dysfunction which surpass those found in many postgraduate texts. In addition, there are accounts of marriage and marital dysfunction, the experience of being a single parent, child abuse and ethological and sociological perspectives on family structure. A further feature is a chapter on the rewards and hazards of medicine as a profession.

The final section considers psychopathology. Classification is based on the DSM-III and introductory chapters discuss biological, psychodynamic and sociocultural factors in the aetiology of mental illness. After a brief overview of biofeedback and behavioural medicine there is detailed consideration of child and adult disorders. The strength of these chapters lies in the successful integration of descriptions of clinical syndromes with illustrative case studies. However, I felt that management issues were not given enough consideration. The chapter on schizophrenia failed to mention the use of depot neuroleptics and the importance of day care facilities in rehabilitation. Although drugs are discussed, they are not comprehensively listed with their side effects, an important omission in a book of this size and price.

This is a large, lavishly illustrated book, with useful references and a good index. It provides a comprehensive and readable account of human behaviour with particularly lucid explanations of developmental and dynamic concepts. As such it is highly recommended and should be purchased by medical school libraries and keen students. It could also be usefully read by trainees starting psychiatry.

JOE HERZBERG, *Senior Registrar in Psychiatry, St. Mary's and the Maudsley Hospitals, London*

Bereavement: Reactions, Consequences and Care. Edited by Marian Osterweis, Fredric Solomon and Morris Green. Chichester: John Wiley. 1984. Pp 312. £20.70.

This report of the Committee on Health Consequences of the Stress of Bereavement of the Institute of Medicine contains the most comprehensive review of the scientific literature on bereavement yet published. The evidence of recent studies of the detrimental effects of bereavement confirms the findings of earlier studies. A minority of bereaved people suffer damage to their physical and mental health. There is agreement that social and emotional support to the bereaved is worthwhile, although disagreement how this should be given.

The strongest chapters are those on epidemiology and on the reactions of children, adolescents and other young primates, the weakest are those concerned with physical and anthropological aspects. The chapter on "Monkeys' Responses to Separation and Loss" is of great interest, showing, among other things, that.... "the more familiar a subject is with the setting confronted following a loss and the more supportive the individuals within it are, the less severe the sustained emotional response will be and the more rapid the recovery." These conclusions apply as well to human infants as to monkeys separated from their mothers.

Attachment theory emerges as the most seminal model for the understanding of grief and its consequences; "biological" explanations look very unsatisfactory. The more we learn about the physical effects of bereavement, the more confused the picture. Speculative attempts to link *in vitro* studies of lymphocyte response to mitogens with measurements of hydroxycorticosteroid levels and susceptibility to tumour formations, leave one blinking.

Considerable attention is paid to "depressive illness" following bereavement. Clayton's studies show that a third of widows report the symptoms of "depressive illness" during the early months of bereavement. However this depression usually improves by the end of the first year and, unlike other "depressive illnesses" does not affect the dexamethasone suppression test. Unfortunately, no systematic trials of antidepressant treatment for "depressive illness" after bereavement have yet been published.

Anthropological studies have much to teach us about cultural influences on mourning, but the chapter on socio-cultural influences is sketchy. The chapters concerned with the care of the bereaved provide much evidence for improving the training of health care professionals and for the introduction of bereavement intervention programmes.

It is a sad reflection on the American scene that the only area in which members of the health care professions regularly associate with bereavement counsellors is in the hospices. Bereavement intervention programmes are subdivided into "mutual support approaches", "hospices" and "psychotherapeutic approaches". No place exists for the kind of programme which has proved most successful in Britain, a closely integrated organisation (Cruse) in which professionals and volunteers, bereaved and non-bereaved, work closely together to provide counselling and social support to bereaved people.

C. M. PARKES, *Senior Lecturer in Psychiatry,*
The London Hospital Medical College

Psychoanalytic Approaches to the Resistant and Difficult Patient. Edited by Herbert S. Strean. New York: Haworth Press. 1985. Pp 140. $19.95.

This book consists of a selection of articles first published in journal form in Vol. 1, No. 4 as *Current Issues of Psychoanalytic Practice*. 1984.

There are seven papers on a selection of topics including therapist's countertransference reactions, individual case reports and theoretical papers on projective identification and the negative therapeutic reaction. The editor's intention was to enhance the therapist's knowledge when faced with patients who are considered difficult to treat.

The paper, which in my view stood out, and addressed the stated theme of this book, is by Finell on Projective Identification. It is a critical review of the term followed by her own ideas on the subject which she illustrates with clinical material. Her view is that projective identification has been considered too narrowly with insufficient attention being paid, either to other mental phenomena that exist side by side with it, such as envy and omnipotence, or to the characteristics of the object into which projection takes place. She suggests that a particular transference counter-transference problem is, that the analyst's sense of omnipotence seems to be gratified by the belief that he can work with such primitive defences, while the patient's envy of the omnipotent analyst remains unanalysed. She goes on to suggest that working through this type of issue contributes to the resolution of stalemated therapeutic situations.

Another article on a related topic the Negative Therapeutic Reaction is a review of the literature by Lane. It has a useful list of references and highlights the different definitions used by different authors who have written on this subject. It is somewhat disappointing due to the author's diffidence about his own conclusions.

There are two further articles which I found of value. Wells Goodrich has written a workmanlike account of his experience and approach in the psychoanalytic treatment of disturbed adolescents resident at Chestnut Lodge. He uses an approach which involves individual, milieu and family therapy. He underlines how these three approaches are integrated and conceptualised in terms of a maturational process from attachment through to eventual individuation.

The final article of merit is a very succinct and highly condensed review article on group processes which are illustrated by a series of clinical vignettes. This is an article by two experienced group therapists Woolf and Kutash.

The papers contained in this book, although of interest are quite disparate and consequently the reader is left with the task of drawing together the useful and relevant elements. Since they have already been published in journal form, one could just as easily select the articles of interest from the original journal.

A. I. GARELICK, *Consultant Psychotherapist*
Claybury Hospital, Essex

General Psychiatry. Edited by H. H. Goldman. Los Altos, California: Lange Medical Publications. 1984. Pp 696. $26.50.

This overview of psychiatry written for medical students is a new recruit to the Lange Library and the editor anticipates that like its stable-mates it will be regularly updated. Its 60 short chapters are written by 54 authors. A conscientious attempt has been made to achieve uniformity of style with clear and frequent sub-headings and the use of many illustrative cases. The early chapters on preclinical background betray the American orientation: a seven page chapter on "Normal Psychological Developments" consists only of a summary of Erikson's theory. Cookbook accounts of Freudian theories of development and defence are provided. Jung is given the same four column inches as H. S. Sullivan. The chapter on clinical interviewing discusses theoretical problems at the expense of stating what information needs to be collected, and although more space is devoted to the clinical summary, this consists only of a single case history devoid of discussion as to the clinical relevance of the material presented.

Clinical chapters use DSM III as their diagnostic framework and it is unfortunate that there is no discussion of the theoretical justification for diagnoses in psychiatry and no mention of the evolution of DSM III and the existence of alternative diagnostic systems such as the RDC and ICD-9. Psychogeriatrics is allocated five pages on "Ageing" and three on "Dementia" which are adequate neither as discussions of diagnostic entities and their pathological basis, nor in offering principles for management. Alcoholism is given nearly twice as much space, but although reference is made to the "CAGE" screening questions, the four questions involved are not described. No guidance is given to dosage in detoxification regimes and no description given of the physical consequences of alcohol abuse. The chapters on the major psychoses are American in orientation. Only United States work on the epidemiology of schizophrenia is quoted and there is no mention on the contribution to diagnosis of the PSE and CATEGO System and none of the work in families of schizophrenics by Leff *et al.* Lithium is stated to be the first line of treatment of acute mania and no mention is made of recent work on monoamine receptor abnormalities in depression. Psychotherapeutic management is discussed over 75 pages, and descriptions both of theory and technique are clear, if somewhat dull. Physical treatment is dealt with much more sketchily; the single page on ECT refers neither to possible mechanisms of therapeutic action nor to recent controlled trials of its use.

Though a few 1983 references are given, the majority of works cited are from 1980 or before. The book is sturdily bound in stiff paper covers, the typeface is clear though small, and there are rather few illustrations or tables which are rather poorly integrated with the text. It is written very specifically for American medical students and the approaches offered both to diagnosis and treatment are likely to mislead students sitting British Final Examinations in Psychiatry. The level of discussion and the references given are certainly inadequate for those sitting the MRCPsych. The basic problem is that too wide an area is covered far too sketchily. I will not be lending this volume to my students.

CORNELIUS L. E. KATONA, *Senior Lecturer in Psychiatry, Middlesex Hospital Medical School. London*

On the Way to Self: Ego and Early Oedipal Development. By Johanna Krout Tabin. New York: Columbia University Press. 1985. Pp 362. $30.00.

In this mature work, Tabin considers psychoanalytic and other psychological data to present a coherent account of complex aspects of early child development. This revolves around her concept of the primary oedipal phase, earlier than the classically conceived oedipal stage. What is new is Tabin's model of the inter-relationship between the many tasks and conflicts a young child faces.

Tabin focuses on the child's second year of life, when many new capacities are acquired, both muscular and cognitive. The primary oedipal complex involves an interplay between 1) awareness of sexual feelings 2) awareness of gender 3) separation-individuation. For the little girl, the component conflicts are (a) sexual feelings for her father lead to rivalry with her mother, on whom she still depends (b) the process of gender based modelling on mother is in conflict with the concomitant process of separation-individuation from mother (c) the price of separation-individuation from mother is the loss of protection and support from mother.

Some of the conflicts are the same for the little boy, but in his case, sexual attraction is towards the very person he is attempting to move away from. In the categorical thought of the two year old, closeness to mother means being like her (female) and therefore not male, yet it is his very maleness that drives him towards her; his sexual desire threatens his gender identity, and conflicts with his separation-individuation moves. Moreover, his sexual feelings for his mother bring him into rivalry with his father on whom is he simultaneously trying to model himself.

The difference between the primary and the classical oedipal phase is that in the latter, many of the early developmental tasks relating to the sense of self are nearer completion; thus the sense of self is more established, and less easily threatened. Tabin suggests that all *gender-specific* pathologies relate to the primary oedipal phase. As an example, she looks in detail at anorexia nervosa. She also considers various common everyday syndromes illuminated by her model; e.g.—men who must dominate women; women who compulsively seek men who will abuse them.

With a truly scientific stance, Tabin discusses the evidence for the primary oedipal phase, comparing other authors' views and also suggesting various tests of the model. Her thesis acts as a corrective to widespread assumptions, especially in the American literature, of a pre-oedipal dyadic phase of development. I feel sure she is correct in arguing that apparently dyadic transferences, when more completely explored, will turn out to exist within triadic fantasies.

This is an original and important book, throwing light on obscure areas of differences between male and female sexuality. I think the ramifications of the model could be explored further into an understanding of perversion and certain narcissistic disturbances where oedipal conflict is by-passed. Moreover, I think greater emphasis could be given to the way in which working through the oedipal triadic constellation is in itself central to the establishment of the sense of self.

PHIL MOLLON, *Regional Psychologist*
in Psychotherapy (Northern Region),
Dryden Road Hospital, Tyne and Wear

Practice of Inpatient Behaviour Therapy: A Clinical Guide. Edited by Michel Hersen. Orlando, Florida: Grune & Stratton. 1985. Pp 291. $34.50.

The concept of inpatient behaviour therapy is relatively new. Even those working in specialised research units might only be familiar with the work done on obsessive-compulsive disorders in an inpatient setting. For this reason alone this book is most welcome and it puts together a wealth of information. It begins with a discussion of general issues concerning aspects of staff training and a description of the medical aspects of care. The bulk of the book is the second part which is concerned with the variety of treatments available using an inpatient setting: these are obsessive compulsive disorders, affective disorders, schizophrenia, alcohol abuse and personality disorders. The two chapters on affective disorders and schizophrenia will be of particular interest to the general psychiatrist carrying out catchment area work, as he may not be aware of the enormous advances made in psychological treatments of these conditions in recent years. Case illustrations give the reader a flavour of these treatments, and the behavioural literature is reviewed in a critical manner. It is refreshing to read that claims are not made for the all-round applicability of behavioural techniques to cases of depression and schizophrenia, but it is made clear that behavioural techniques are part of the therapeutic armamentarium with which psychiatrists managing these common problems should be familiar. There is a stress on the interface between pharmacological and psychological treatments, as well as an emphasis on the increasing sophistication of behavioural treatments, for example, the use of family resources to improve the outcome in schizophrenia. The chapter on alcohol abuse deals with the heated controversy over the value of teaching controlled drinking as well as reviewing more accepted treatments such as Antabuse.

The third section of the book concerns the treatment of children and adolescents, and includes chapters on acting out disorders, pervasive developmental disorders, eating disorders and paediatric medical problems.

Somehow or other the editor has managed to weld together contributions from 25 authors, mainly psychologists, into a satisfactory whole which recommends itself for all psychiatric libraries.

RICHARD STERN, *Consultant Psychiatrist,*
St George's and Springfield Hospitals, London

The Therapeutic State: Psychiatry in the Mirror of Current Events. By Thomas Szasz. Buffalo, New York: Prometheus Books. 1984. Pp 360. $22.95 (hb), $10.95 (pb).

In this latterday *Book of Lamentations*. Szasz has brought together 75 of his own articles published largely in magazines and journals for general readership over the last twenty years. His articles have usually been stimulated by some extreme of the US political, legal or psychiatric scene (and there have been some wonderful extremes in the last twenty years) or by the request for a book review.

His sustained invective makes tiring reading since one is constantly being stimulated to answer back. One is annoyed by his presumption that he is the only 'free man of medicine'—the one who is morally right in his opinions about difficult issues of freedom and justice. One is annoyed at how logical he can be, yet missing the spirit of our endeavours. One is annoyed that he ignores or obfuscates valid opposing arguments, especially in articles aimed at ill-informed lay audiences. One is annoyed when he *always* uses 'lobotomy' instead of 'leucotomy', when he falsely extrapolates from malingering and hysteria to schizophrenia, when he says 'disease of the brain would have to manifest itself by neurological signs, not psychiatric symptoms'. One is then annoyed when he gets it right.

And he does get it right at times. His views on the response of medicine and society to drug addiction carry great validity at this present time of political hysteria about the issue. His highlighting of the tardy response of Western psychiatrists (including many in this country) to Russian abuses was timely. His protestation against the over-usage of psychiatric testimony, both to put people away and to free them from legal responsibility is a worthwhile counter measure. He has a talent for needling psychiatry's soft-spots.

He is also very amusing at times. His comparison of the gobbledegook spoken by a past President of the American Psychiatric Association with the thought disorder of schizophrenia is brilliant fun. His barbed review of books by Laing and Cooper is spot-on.

Szasz is often called a gadfly, but he strikes me as more like some persistent, unsquashable mosquito, determined to get at the jugular whether his victim deserves it or not. His book does deserve to be read for its tireless championing of a single-minded 'libertarian' approach, even though at times this flies in the face of reason and commonsense.

JONATHAN M. BIRD, *Honorary Senior Registrar, Maudsley Hospital, London*

Treatment of Mental Disorders. Edited by John H. Greist, James W. Jefferson and Robert L. Spitzer. Oxford: Oxford University Press. 1982. Pp 548. £28.00 (hb), £15.00 (pb).

The title of this handsome volume suggests that with its help specialists and non-specialists alike will be able to choose optimal treatment for all their patients with mental disorders. Close tie-up of treatment with the DSM III diagnostic system is still more seductive: with its help, reliable cookbook approach to assessment as well as treatment will be within our grasp. Sadly this promise is largely unfulfilled. There is little uniformity of style among the 27 contributors and although the DSM III framework is rigidly adhered to there is very little discussion of the problems of DSM III pigeon-holing. Schizoaffective disorder for example is granted only a page because DSM III regards it as a residual category despite the clinical reality that there are special problems in the treatment of patients in whom schizophrenic and affective symptoms co-exist. Unlike the rest of the book, the chapter on organic psychoses offers useful guidance on principles of assessment prior either to diagnosis or treatment. It is perhaps surprising that in a book devoted to treatment, studies of neotropics and acetylcholine precursors in dementia, however disappointing the results to date, are hardly mentioned. Throughout the book, drug treatment is discussed in greater depth and detail than psychotherapeutic principles of management, but possible mechanisms of therapeutic action are hardly touched on.

Somewhat unusual priorities of space are adopted: 98 pages on substance induced disorders, more than to affective disorders and schizophrenia combined, and 64 pages on sexual dysfunctions and perversions. The weaknesses of the editorial approach are best seen in the chapter on affective disorders. The linkage to DSM III subtypes is so rigid that though the discussion of treatment goals and the assessment of suicidal intent is sound, there is no opportunity for overall consideration of treatment strategies in depression. There is no discussion of recent placebo controlled trials of ECT and none of predictors of ECT response: indeed the concept of "endogenicity" is not mentioned in either the chapter nor the index. Neither new generation antidepressants nor drug combinations in resistant depression are covered, and cognitive therapy for depression is dismissed in 13 lines. The chapter on schizophrenia provides an interesting treatment flow-chart concentrating mainly on drug therapy, though the work of Leff *et al* on expressed emotion is briefly reviewed as is the evidence for the role of psychotherapy in schizophrenia. Long-term risks of neuroleptic treatment are touched on very briefly.

The book was published in 1982 and its references are understandably somewhat out of date by now. More important, the basic premise inherent throughout is that it is possible, given a diagnostic system, to provide treatment recipes without discussion either of the adequacy of the particular diagnostic system or of possible mechanisms of treatment response or treatment failure. I think that this premise is mistaken, and although the book is attractively produced and by no means exorbitant in price I cannot recommend it either to libraries or to individual readers.

CORNELIUS L. E. KATONA, *Senior Lecturer in Psychiatry. Middlesex Hospital Medical School, London*

Current Approaches to Down's Syndrome. Edited by David Lane and Brian Stratford. Eastbourne: Holt Rinehart & Winston. 1985. Pp. 435. £19.95.

This book is well produced and clearly written. It is a collection of essays by authors from the different disciplines which provide services for the mentally handicapped. The contributors are drawn from a number of different countries, including the USA, Australia, Eire, West Germany, Poland, and Canada. The 21 chapters are divided into four parts.

First is a brief summary of the social and historical context by Tony Booth who is a lecturer in education at the Open University. The sub-title for his chapter is 'Labels and their consequences'. The second section of the book is devoted to physical aspects of Down's syndrome and is followed by another on educational aspects. The final section is headed 'Life Chances'. Rex Brinkworth has the last word in a chapter headed 'Possibilities and Achievements'. He is best known as the founder, in 1970, of the Down's Babies Association, now known as the Down's Children's Association. In his chapter he argues that, in planning for the future of a Down's child, it is better to err on the side of cautious optimism rather than miss educational and social opportunities through unjustified pessimism.

This book is intended for all the members of the contemporary multi-disciplinary team. The authors have largely achieved this aim and, for example, Hallidie-Smith's chapter on the heart in Down's syndrome uses very clear diagrams to illustrate the variety of developmental anomalies which are especially common in the syndrome. David Silverman, a sociologist, considers families attending a paediatric cardiology unit. His chapter is headed 'Agreeing not to intervene: doctors and parents of Down's syndrome children at a paediatric clinic'. Silverman tries to make an objective analysis of the process whereby doctors and parents together may reach an agreement not to operate to correct a congenital heart defect. Hallidie-Smith accepts that about half of Down's babies have a heart defect and uses a diagram to illustrate the great difference in life expectation when compared with children without this additional problem. She considers that in general a case can be made for surgical closure of a large ventricular septal defect causing symptoms in a Down's child of one year or less, but not later because irreversible damage will already have been done to the lungs. She accepts that there is a 20 per cent mortality in operations for the closure of a complete atrioventricular canal in a Down's child under two years.

Jacek Zaremba contributes an excellent chapter on recent medical research in this field. He is rightly cautious about accepting a paternal age effect in causation though the error clearly stems from the father in a minority of cases. He also expresses reserve about the claim that oral contraceptives may increase the incidence of Down's syndrome. This book can be strongly recommended for all professional workers dealing with mental retardation.

BRIAN KIRMAN, *formerly Consultant Psychiatrist, Queen Mary's Hospital for Children, Carshalton*

Wounds of War: The Psychological Aftermath of Combat in Vietnam. By Herbert Hendin and Ann Pollinger Haas. London: Harper & Row. 1985. Pp 267. £18.75.

Post-Traumatic Stress Disorder and the War Veteran Patient. Edited by William E. Kelly. New York: Brunner/Mazel. Pp 338. $30.00.

These books with a similar theme are concerned with psychological changes in structure, style and aim. Both are sincere works devoted to explaining the enormous problems generated at the time, and often persisting still. *Wounds of War* is for the intelligent lay reader and is largely devoted to the search for meaning in the psychological effects of battle. It highlights ways in which the strain of the Vietnam war front was unique, explaining the suffering of veterans in terms of stress, personality and background, illustrated by lengthy case histories accompanied by psychodynamic insights. The treatment process is seen essentially in terms of psychotherapy.

Post-Traumatic Stress Disorder and the War Veteran Patient embraces the work of 19 psychiatrists, psychologists, social workers, nurses and educationalists, covering the evolution of "PTSD", the nature of stressful events, readjustment, problems of the black veteran, and a firm approach to the prediction of breakdown. Many of the chapters are devoted to treatment, including not only specific therapies, but also nursing care and in-patient programmes. Emphasis in treatment is essentially psychodynamic with hypnosis for elicitation.

One problem common to both, and discussed more fully in the second work, is the imposed labelling of all adverse psychiatric, psychological or social sequelae of war veterans as post traumatic stress disorder, thereby risking assumptions that they have similar clinical psychological and physiological qualities and therapeutic responsiveness. A further assumption is that war stress, as recognised by the servicemen from spontaneous or stimulated memory, is the cause. This would be perhaps a useful starting point if the conditions were prominent during battle or very shortly afterwards, but it is difficult to accept such an aetiological link in some examples when several or even many years have passed. It is disappointing in the light of military history to see no general mention of the effect of sleep loss, disturbance of biological rhythms, infections, feeding changes and grief from loss of civilian support.

The very size of the problems and other unusual circumstances of Vietnam may explain the choice of methods used in treatment, but the reader is left to ponder whether special circumstances produce unusual mental or behavioural reactions, whether excitatory abreaction has been electively abandoned in favour of less active methods, and if for the shell-shocked there was a possibility for provision of a period of semi-narcosis in the acute stage.

The authors and editors are to be congratulated in treating, in a medical framework, matters so intertwined in emotion and politics. Both books succeed in leaving a lasting impression and a broad front for thought. Neither is bedside reading.

JOHN POLLITT, *Consultant Psychiatrist,*
St Thomas's Hospital, London

Comprehensive Textbook of Psychiatry/IV Edited by Harold I. Kaplan and Benjamin J. Saddock. London: Williams & Wilkins. 1985. Pp 2054. £132.00 (2 volume set): £120.00 (1 volume set).

In 1967 the first edition of this most impressive textbook broke new ground in that it contained detailed biological, psychological and sociological material relevant to psychiatry—in addition to the systematic treatment of the various disorders which constitute the traditional psychiatric text. This 'comprehensive' approach has continued to be one of the work's distinguishing characteristics and the current edition contains superb chapters on a wide variety of topics, knowledge of which, according to the editors, is "prerequisite for clinical competence". These include sections on genetics, psychopharmacology, anatomy and physiology of the nervous system and clinical psychology. There is also a great deal of useful information on medical conditions, ranging from an unusually good account of diseases of the nervous system to a concise description of the Heimlich manoeuvre.

The fourth edition has been thoroughly revised and considerably shortened. Whole sections from previous editions have been deleted and some new ones added—including excellent contributions on cognitive therapy, short-term dynamic psychotherapy, the biochemistry of affective disorders and the evaluation of DSM—III. Though shorter than previously, it still contains more than two million words, and if reduplication of material were avoided, the text could be reduced further; for example, there are two equally excellent accounts of narcolepsy (and another very good one), two on culture-bound syndromes, and at least two each on anorexia and bulimia nervosa and on defence mechanisms.

This book is unashamedly American: of the 186 contributors more than one-quarter are based in New York and, apart from less than a handful who have posts in Canada, the remainder work in the USA; not a single contribution comes from the rest of the world. It is no wonder then that British readers might observe some American biases: the emphasis on psychodynamics in discussing neurotic disorders, the rather inadequate treatment of phenomenology, the importance attached to signs such as 'blunting of emotional response', 'loosening of associations', 'bizarre behaviour' and 'the praecox feeling' in the early diagnosis of schizophrenia, the discussion of the legal concept of 'valid informed consent' and the occasional sky-scraping Americanism such as "on the part of patients and their significant others".

Despite these criticisms the work is truly outstanding and can be recommended thoroughly to all psychiatrists, including those preparing for the MRCPsych examination. A major drawback is its high cost and I have yet to meet a trainee who would be prepared to spend £120 on it. Perhaps librarians and tutors might note that this textbook is very probably the best on psychiatry in the English language; need one say more?

KENNETH GRANVILLE-GROSSMAN,
Consultant Psychiatrist, St Mary's Hospital
and the Royal Masonic Hospital, London

Child Psychiatry for Students. 3rd edition. By F. H. STONE and C. KOUPERNIK. Edinburgh: Churchill Livingstone. 1985. Pp. 124. £5.95.

What is important about child psychiatry is how teachers can engage the interest of medical students in a specialty which may not appeal to them immediately but which will be of importance in the future especially to those who go into general practice. This book is written in clear, concise language, with a glossary for inescapable words and phrases. It gives a vivid, empathic account of the problems of child development, both normal and abnormal and suggests how those concerned with helping troubled children and their families can and should be involved.

It is obviously the distillation of long-term day to day contact with children, and the evidence on which statements are made is cited. The references are clear, concise and not overwhelming. The book should be required reading for all undergraduate students in paediatrics and child psychiatry.

ANNE BOLTON, *Consultant Child Psychiatrist,*
The Middlesex Hospital, London

AMERICAN JOURNAL OF PSYCHIATRY

Volume 143, Number 2 **February 1986**

Special Articles

131 Diagnosis-Related Groups and General Hospital Psychiatry: The APA Study *Joseph T. English, Steven S. Sharfstein, Donald J. Scherl, Boris Astrachan, and Irvin L. Muszynski*
140 Genetic and Clinical Implications of Alcoholism and Affective Disorder *Marc A. Schuckit*

Regular Articles

148 Consumers' Views of *DSM-III*: Attitudes and Practices of U.S. Psychiatrists and 1984 Graduating Psychiatric Residents *V. Chowdary Jampala, Frederick S. Sierles, and Michael Alan Taylor*
153 Childhood Parental Death and Adult Psychopathology *Paul V. Ragan and Thomas H. McGlashan*
158 Secondary Morbidity Among the Recently Bereaved *Vincent Mor, Colleen McHorney, and Sylvia Sherwood*
164 How to Write a Psychiatric Report for Litigation Following a Personal Injury *Brian F. Hoffman*
170 Process Analysis of Judges' Commitment Decisions: A Preliminary Empirical Study *Harold Bursztajn, Thomas G. Gutheil, Mark Mills, Robert M. Hamm, and Archie Brodsky*
175 Comparison of PET Measurement of Local Brain Glucose Metabolism and CAT Measurement of Brain Atrophy in Chronic Schizophrenia and Depression *Arthur S. Kling, E. Jeffrey Metter, Walter H. Riege, and David E. Kuhl*
181 Symptom Correlates of Vulnerability to Backward Masking in Schizophrenia *Michael Green and Elaine Walker*
187 Psychoactive Substance Use Among Medical Students *James F. Maddux, Sue K. Hoppe, and Raymond M. Costello*

Commentary

192 Divorce and Child Custody Resolution: Conflicting Legal and Psychological Paradigms *John W. Jacobs*

Editorials

198 Psychiatry, Medicare, and Prospective Payment *Shervert H. Frazier, Howard H. Goldman, and Carl A. Taube*
201 *DSM-III* and Psychotherapy *Paul Chodoff*

Brief Communications

203 Elderly Schizophrenic Inpatients in the Wake of Deinstitutionalization *Ann B. Goodman and Carole Siegel*
207 Is It Normal for Terminally Ill Patients to Desire Death? *James Henderson Brown, Paul Henteleff, Samia Barakat, and Cheryl June Rowe*
211 Schizotypal Symptoms in Patients with Borderline Personality Disorders *Anselm George, and Paul H. Soloff*
215 Masochistic Personality: An Empirical Study *Frederic Kass, Roger A. MacKinnon, and Robert L. Spitzer*
218 Digitalis Intoxication Misdiagnosed as Depression by Primary Care Physicians *Frederick S. Wamboldt, James W. Jefferson, and Marianne Z. Wamboldt*
221 Social Class and Psychiatric Outcome *Thomas E. Gift, John S. Strauss, Barry A. Ritzler, Ronald F. Kokes, and David W. Harder*
225 Psychological Benefits of Spiritual Baptist "Mourning," II: An Empirical Assessment *Ezra E. H. Griffith, George E. Mahy, and John L. Young*

Clinical and Research Reports

229 Memory Deficits and Anticholinergic Levels in Chronic Schizophrenia *Deborah Perlick, Peter Stastny, Ira Katz, Meredith Mayer, and Steven Mattis*
231 Relationship Between Age and Incidence of Parkinsonism in Psychiatric Patients Treated with Haloperidol *Peter Moleman, Gerlof Janzen, Berta A. von Bargen, Evert J. Kappers, Lolke Pepplinkhuizen, and Paul I. M. Schmitz*
234 Preliminary Evidence for the Utility of Carbamazepine in Alprazolam Withdrawal *Ehud Klein, Thomas W. Uhde, and Robert M. Post*
236 The Effect of Age on Dexamethasone Suppression Test Results in Alcoholic Patients *William H. Nelson, Pamela Sullivan, Arifulla Khan, and Ravikiran N. Tamragouri*

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Index to Advertisers

Pharmaceuticals

The Boots Company plc	*facing* p 305
Brocades Limited	p ii
Janssen Pharmaceuticals Limited	*facing* p 278
Labaz	*facing* p 279
May & Baker Limited	*facing* p 274
E. Merck Limited	*facing* p 316
E. R. Squibb & Sons Limited	*facing* p 275 and 304
Upjohn Limited	*facing* p 278

Surgical and Medical Appliances

J. J. Electronic Components Limited	p ii

Clinics, Hospitals and Nursing Homes

Bowden House Clinic	p iv
The Retreat	*inside back cover*
Ticehurst House Hospital	p iii

Booksellers and Publishers

American Psychiatric Association	*facing* p 317
William Heinemann Medical Books	p iii
International Journal of Therapeutic Communities	*loose insert*

Miscellaneous

Charing Cross and Westminster Medical School	p ii
Northern European Epilepsy Meeting	*facing* p 317

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THE BRITISH JOURNAL OF PSYCHIATRY

March 1986 Volume 148

Lecture

Socio-Psychiatric Aspects of the Young Severely Mentally Retarded and the Family (19th Blake Marsh Lecture, February 1985); *Annalise Dupont* 227

Review Article

Volatile Substance Abuse: A Review of Possible Long-Term Neurological, Intellectual and Psychiatric Sequalae; *Maria A. Ron* 235

Papers

Political Hazards in the Diagnosis of 'Sluggish Schizophrenia'; *Harold Merskey and Bronislava Shafran* 247

The Endogenous Sub-type of Depression: A Study of its Internal Construct Validity; *Michael A. Young, William A. Scheftner, Gerald L. Klerman, Nancy C. Andreasen and Robert M. A. Hirschfeld* 257

The Depressive Symptoms of Bulimia Nervosa; *Peter J. Cooper and Christopher G. Fairburn* 268

The Diagnosis of Schizophrenia by Language Analysis; *William I. Fraser, Kathleen M. King, Philip Thomas and Robert E. Kendell* 275

The Impact of Individual and Family Treatment on the Affective Climate of Families of Schizophrenics; *Jeri A. Doane, Michael J. Goldstein, David J. Miklowitz and Ian R. H. Falloon* 279

Early Life Events and Affective Disorder Revisited; *C. Faravelli, E. Sacchetti, A. Ambonetti, G. Conte, S. Pallanti and A. Vita* 288

The Evaluation of Illness Behaviour and Exaggeration of Disability; *J. R. Clayer, C. L. Bookless-Pratz and M. W. Ross* 296

The Influence of Seizure Type and Medication on Psychiatric Symptoms in Epileptic Patients; *S. W. Brown, M. E. L. McGowan and E. H. Reynolds* 300

Cross-National Invariance of Dimensions of Parental Rearing Behaviour: Comparison of Psychometric Data of Swedish Depressives and Healthy Subjects with Dutch Target Ratings on the EMBU; *Willem A. Arrindell, Carlo Perris, Hjördis Perris, Martin Eisemann, Jan Van Der Ende and Lars von Knorring* 305

Mortality and Facial Dyskinesia; *H. A. McClelland, D. Dutta, A. Metcalfe and T. A. Kerr* 310

Hypothyroidism as a Correlate of Lateral Ventricular Enlargement in Manic-Depressive and Neurotic Illness; *Eve C. Johnstone, D. G. C. Owens, T. J. Crow, N. Colter, Claire A. Lawton, R. Jagoe and L. Kreel* 317

Brief Reports

Anniversary Reactions; *E. B. Renvoize and J. Jain* 322

Folie à Deux in Identical Twins: Interaction of Nature and Nurture; *Arthur Lazarus* 324

Normal Dexamethasone Suppression Test in Obsessive-Compulsive Disorder; *W. Monteiro, I. M. Marks, H. Noshirvani and S. Checkley* 326

Books Reconsidered

The Discovery of the Asylum: David J. Rothman, J. L. T. Birley 330

Correspondence 332

Book Reviews 345

Notice to contributors, subscribers and advertisers inside front cover

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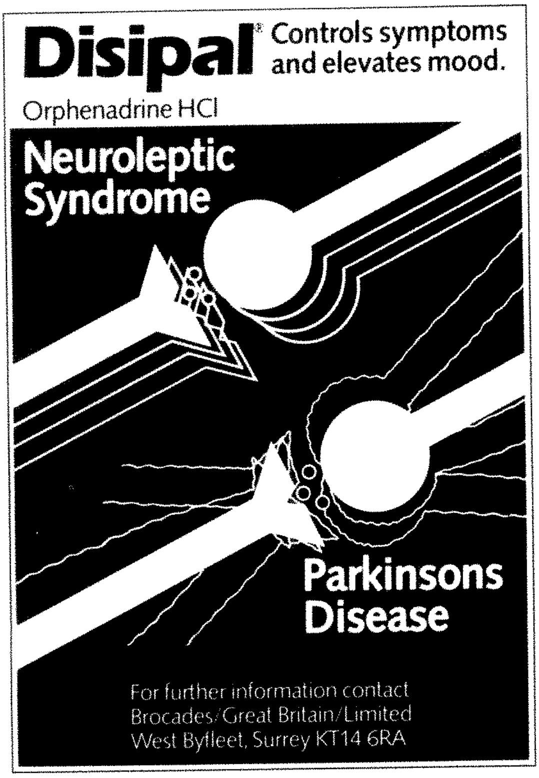

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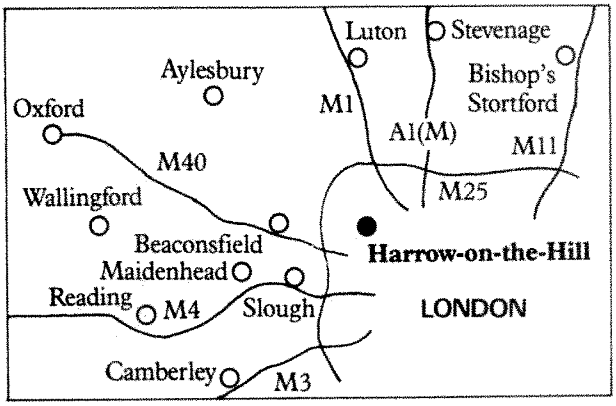

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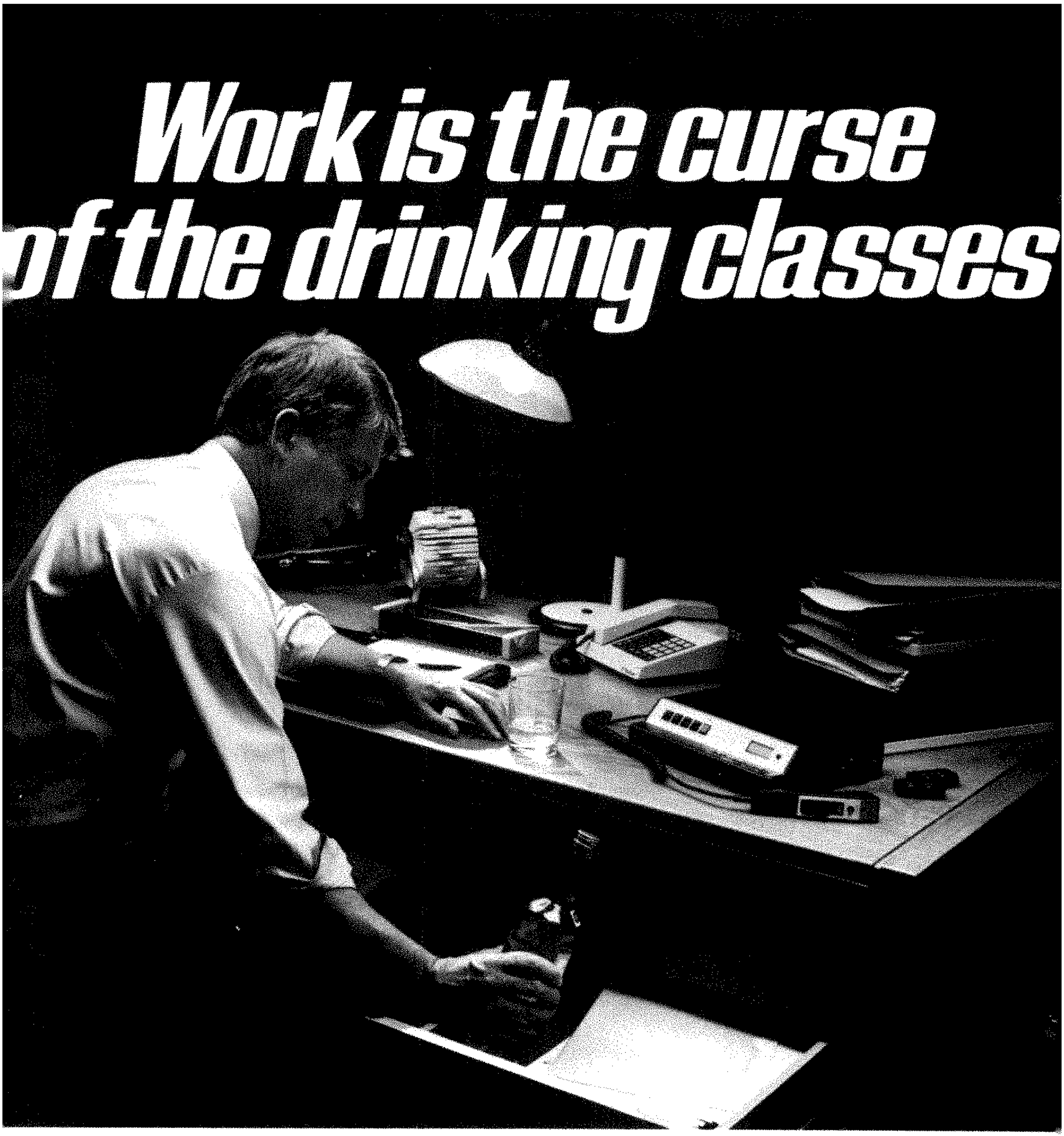

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(1) Azrin, N.H. (1976) *Behav. Res. & Therapy.* **14**:339
(2) Robichaud, C. et al. (1979) *ibid.* **17**:618
(3) Gerrein, J.R. et al. (1973) *Arch. Gen. Psychiatry.* **28**:798

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Annotation

Treatment of Prolonged Combat Reaction

A. BLEICH, R. GARB and M. KOTTLER

Combat reaction is a clinical entity which is classified under one of the most complex diagnostic formulations in modern psychiatry-post-traumatic stress disorder (PTSD). Of all the life experiences which may create trauma, war-related stress seems the most complicated and difficult to understand. Despite an abundance of clinical observation, this has been considered from such differing theoretical perspectives that a comprehensive therapeutic conceptualisation has proved elusive.

Post-traumatic disorder (DSM III, 1980) is a new category which delineates a syndrome developing after a discrete traumatic event in a stress setting. These diagnostic criteria have demonstrated their reliability in casualties suffering from combat reaction, and many publications have been generated around the concept, including major work carried out in Israel at the Mental Health Centre of the Israel Defence Force (IDF) by Solomon, (1984). In characterising the syndrome so clearly in its clinical aspects, and defining its link to the traumatic cause, one of the basic goals of the diagnostic process was accomplished: the improvement of communication between professionals. However, the question remains, as to whether other important goals of diagnosis have also been enhanced, such as the achievement of a rational therapeutic policy.

Diagnostic conceptualisations which tie PTSD to stress and trauma invariably involve two different approaches from two different theoretical bases: the concepts dealing with trauma on the one hand, and those dealing with stress/response theory on the other.

Trauma and analytical theory: The broad approach

Trauma as a psychiatric term is borrowed from ancient Greek surgical terminology, meaning an injury stemming from the penetration of the body defence (intactness) such as skin. Freud (1921) saw in psychological trauma an analogy to the surgical concept, an event of such enormous emotional intensity that it breaks through the ego defences and floods it with an uncontrollable anxiety.

The modern psychiatric concept emphasises the objective aspect of the traumatic event, which is required to be outside the normal range of ordinary human experience; undoubtedly, war traumas fall well within this definition. Freud, together with the generation, who witnessed the horrors of World War I, verified in work with soldiers the dynamic configuration of combat stress disorders. Kardiner & Spiegel (1947), following World War II, corroborated these impressions; they saw in the dynamic conflict between abreaction and repression, the fundamental shaping core of the post-traumatic stress reaction.

Thus, a man who undergoes a traumatic experience, characterised by intense anxiety and feelings of helplessness regarding the danger of extermination, feels the need to integrate the threatening event. He then needs to undergo a corrective experience before being able to return to normal function. Since the actual trauma is in the realm of the past, he is only able to struggle with memories. The repetitive re-experiencing of the traumatic events by thoughts, mental images, and nightmares, is in fact an expression of a kind of natural abreactive process. On the other hand, the mental pain involved in the replication of the trauma pushes towards its repression. The mental resources invested in continuous repression or avoidance of any event or situation reminiscent of the trauma undermines the functional ability of the ego, and causes a decline in involvement with the external world. This manifests itself in decreased interest in, and interpersonal capacity for communication, as well as reduced affective response and a progressive decline in general function.

The term post-traumatic neurosis, or combat neurosis, originates from the analytical notion which sees in the trauma an entity for repression (primary gain), and subsequently causes the development of secondary symptomatic behaviour with symbolic and adaptive meaning (secondary gain).

This approach therefore will consider encouragement of the abreactive process as an essential and central element of therapy. Therefore, treatment aims to reconstruct the trauma, together with its attending emotions, in such a way as to allow the casualty to grapple with them. He is now, in therapy, able to cope with frightening emotions such as guilt, loneliness, anxiety, and grief which previously threatened to overwhelm him. The individual predisposition for the development of post-traumatic neurosis was explained by Freudian theory as a repetition compulsion for infantile traumas of childhood, i.e. the interpretation of the event as traumatic at a later age stems from reactivation of earlier and incompletely worked through traumas.

Balson & Dempster (1980) and others described success in treating post-traumatic war casualties by using hypnotherapy for abreactions. When the abreactive process was completed, the forbidden unconscious wish was identified and interpreted to the patient. The process was repeated under conditions of full alertness, and enabled full working through and understanding of the adaptive value of the symptoms and the capacity for change.

However, ongoing work with post-traumatic patients, especially combat reaction casualties has somewhat negated the seemingly essential link to early childhood trauma (Kardiner, 1947; Hocking, 1970; Hendin, 1983). In a modified variation of the dynamic theoretical model, the major focus has been shifted onto the role of recent trauma, during which mental resources enabled coping only by massive repression, thereby permitting continued function. However, the greater mental energy invested in such repression reduces future coping capacity; consequently, an event, sometimes of seemingly minor significance in objective terms, takes on sufficient subjective meaning to cause severe post-traumatic stress disorder. Work in Israel with PTSD casualties in the recent war has illustrated some cases in which the traumatic contents actually originated in former wars.

Despite the common themes which appear in dynamic therapy, differences do exist in the emphases placed by various writers on differing foci. Kardiner (1947), for example, claimed that it is not the abreaction, but the reconstruction of the traumatic event, together with the replication of the experience, that constitutes the main therapeutic ingredient. He described successful short-term therapy in two post-traumatic patients, six to seven years after their war experience, wherein great emphasis was placed on the precise replication of the trauma until the patient could withstand the experience. Subsequently, with the help of the therapist, the link between present problems and the traumatic event was worked through. Horowitz (1974) also includes cognitive elements in the dynamic approach, and offers what he considers to be a new dynamic equation as being at the centre of the PTSD—intrusiveness versus denial.

Intrusiveness is manifested in the compulsive experience of thoughts, images, and dreams related to the traumatic event. Opposed to this is the denial of the meaning of the trauma and its consequences. In therapy, the patient is helped to cope with the traumatic memories and to transfer them from an actively troublesome and painful dimension to a more integrative mode, where they are experienced in a more passive and controlled fashion, within the process of acceptance. With the aid of the therapist, the patient is able to examine the traumatic event and its specific meaning for him; both come to identify hidden conflicts, activated by association to that traumatic event and its current ramifications. The patient learns to locate the defensive pattern that made him vulnerable to traumatisation, and tries to adopt more adaptive patterns that enable control. Abreaction treatment, with emphasis on reconstruction of the traumatic event, is reserved by Horowitz only for those cases where there is a severe avoidance pattern. Hendin (1983) underlines the importance of understanding the specific meaning of the traumatic event for the person as being the essence of psychotherapeutic treatment, because it is the key to existential change in the way the person sees himself and the surrounding world, and to understanding his mental pain and its related symptomatology.

Theory of stress and coping as a basis for behavioural cognitive treatment

An essentially different approach is based on the concepts of stress and coping. A stress situation is regarded as an expression of the threat posed by any element on the equilibrium of the organism. This may then activate a coping mechanism to reduce stress and return to equilibrium. The origin of potential stress includes, in addition to physiological stress, both mental and social pressures (Titchner & Ross, 1976).

Despite general consensus regarding the influence of stress on the mental and physiological spheres, there are disputing opinions as to the specific effect of intensity and duration. Parallel to those who claim that stress influences are temporary ('evaporating stress'), there are those who believe that stress influences tend to remain and may indeed leave mental scars ('residual stress') (Figley, 1978).

The overwhelming weight of experience accumulated from various studies points to overall general pressure as the main cause of acute combat reaction, rather than personality factors, which have little influence on the acute stage Hoking (1970).

Conceptualising the disorder as being a response to stress has clear therapeutic implications. The assumption conveyed to the patient is that he is basically healthy and that the pressure that cracked him could have broken anyone: '... every ordinary person has his own breaking point under pressure' (Grinker & Spiegel, 1945). Therapy is centred not on intrapsychic processes as in the dynamic model, but on coping processes and strategies aimed externally—the external, real pressure. Internally, it deals with the mental and cognitive accompaniments of the inability to cope with breakdown under pressure. Treatment concentrates on the causes of stress and the patient's responses, attempting to identify the coping mechanisms that were used, and to determine why they failed and how they could be reworked optimally to prevent distress in the future. The therapy is brief, planned, reality orientated, and by definition supportive and positive, with the use of cognitive and behavioural techniques. Its application in forward and rear echelons, in cases of acute combat reaction, proved significantly beneficial, (Nardi, 1983).

Clinical experience with prolonged combat reaction has demonstrated that there is also a place for behavioural therapies which have proven efficacy in common functional problems such as phobic syndromes, sexual difficulties, rehabilitation problems, etc.

An integrative multi-dimensional approach

Delayed or chronic post-traumatic stress disorder is a more complex and difficult therapeutic problem. In contrast to the acute phase, where pressure was the cardinal factor in the pathogenesis of breakdown, here considerably more weight is given to personality elements (Balson, 1980; Hendin, 1983; Alon, 1983; Horowitz, 1974).

However, it would appear that both theoretical approaches outlined above—the conservative dynamic one focusing on intrapsychic process and personality elements on the one hand, and the alternative approach dealing with stress and coping from the cognitive and behavioural aspect on the other—miss the existential aspect. Without this aspect, it is difficult to see how a proper understanding of combat reaction could be reached. This is especially true in the context of Israeli reality, where return to health means return to full participation in military life and a new threat to existence.

The complete existential outlook of the patient includes meaningful life categories such as family, society, work etc., with damage in each category directly influencing the patient's condition. Alon (1983) illustrates the point with a typical family scenario: as a response to the pain and difficulty expressed by her traumatised husband, the wife tries to relieve him by undertaking extra responsibility. The husband understands this as indicating disbelief in his strength and ability, and he responds with fear, depression, and further decline in function, thereby increasing the load on his wife. She soon realises that the more she tries to help, the worse he becomes. A vicious circle is created, fed by rage, despair, and mutual alienation. Children, threatened by the new family situation, find it difficult to accept the passive, alienated, and peripheral father, and may respond symptomatically in one way or another that increases their rejection by him in a typical pathogenic cycle (Garb & Kutz, 1980). A chain of similar dynamic responses may occur in other spheres, causing compounding damage to the self-image of the combat casualty as a family-man, friend, worker, etc. This creates a deepening and fixation of the existential rift, so that the patient frequently entrenches even deeper into his shaky world. Sometimes, this is out of profound despair, depression, and passive acceptance of the situation, but at other times a somewhat different position is adopted. This more problematic attitude is one of the victim projecting onto those around him (including the therapist) blame and responsibility for his situation, with frequent demands for the invalid's right to compensation. This attitude makes it difficult for the therapist to forge a therapeutic alliance. In an interesting strategy, based on the paradoxical approach of Milton Erickson, the therapist places himself in a position 'one down' to the patient; he thus forces the patient to credit any improvement to himself alone (Alon, in press).

A comprehensive therapeutic approach would require the therapist to consider several different aspects, which together constitute the disorder. The most immediate suffering lies in the post-traumatic symptomatology of anxiety, nightmares, moods, etc. A therapeutic approach to these symptoms is possible from any psychotherapeutic stance or from a strictly medical basis. Prompt amelioration of these symptoms would quickly enhance the therapeutic alliance, together with motivation for continued therapy.

The extended time-lapse after the trauma and the organisation of the patient's changed world-view around the post-traumatic state usually prevents a quick, direct approach to the traumatic element itself. There are different emphases in therapy at this stage; undoubtedly, emotional cognitive reconstruction of the trauma is central, but not as a goal in itself, and not in every case. The therapist should decide as to the need, the place, and the rate of this abreactive process in treatment. It is important to understand the individual meaning of the traumatic experience, and to expose the links between the trauma and present difficulties. The achievement of this goal allows the patient to forgive and accept himself on the one hand, and on the other to identify the source of the injury, and to improve his coping patterns and ability to control his life.

We have already described the reciprocal relationship within the family in the deterioration of the situation, and it seems to us that intervention at the family level is essential for achieving significant change. Such intervention is possible at any stage, but is most efficient after some improvement in self-image is achieved.

Freud himself elaborated on the importance of work in the life of man. Continuous contact with reality, with a clearly demarcated place in society, allows self-gratification and dignity, so that a solid and fulfilling occupation is imperative to the success of therapy. The choice of occupation should be a central therapeutic goal and indeed, often becomes a meaningful axis for change and improvement.

It is often possible to sense that a particular case suits a particular clinical and theoretical approach, and natural to pursue a line of therapy determined by such constructs. However, prolonged battle reaction is usually a complex, multi-dimensional problem. Taking the comprehensive view, there is no proven advantage to any particular psychotherapeutic school. The therapist needs to have a broad, comprehensive, flexible outlook, both in the use of therapeutic techniques and in the system within which he wishes to direct his therapeutic efforts.

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Lt. Col. A. Bleich, MD, *Senior Psychiatrist, Israel Defence Force (IDF), Commanding Officer, Central Mental Health Clinic, IDF, Head of Post-Trauma Clinic, IDF.*

*Dr. Ronald Garb DPM, FF Psych, *Consultant Psychiatrist Shalvatah Mental Health Centre, Head of Psychiatric Service, Meir General Hospital, Kfar Saba. 44281, Israel. Sackler School of Medicine, Tel Aviv University.*

Lt. Col. M. Kottler, MD, *Chief Psychiatrist, IDF.*

*Correspondence

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Lecture

Mindlessness and Brainlessness in Psychiatry*

LEON EISENBERG

The theme of this address—that brain and mind are as warp and woof in the fabric of psychiatry—may seem so much a truism as to be a banal choice. I think not. Despite the lip service paid to brain-mind integration, its implications are daily contravened in both theory and practice. At least, this is so in the country where I reside. If the problem is more extreme in the States, as most everything seems to be, recall the words Sir Aubrey Lewis (1953) wrote in commenting on Anglo-American contrasts, some 30 years ago: "the chief differences between your psychiatric scene and ours are differences only of quantity and tempo." Think of me, then, as an anthropologist describing an exotic foreign culture and reporting on the strange customs of the natives, in hope of shedding light on your own.

Before joining my guided tour, you may wish to calibrate your compass, in order to correct for the extent to which mine deviates from what you hold to be true North. My lodestone is Adolf Meyer as interpreted by Leo Kanner (1933). With Meyer (1912), I reject both "the neurologizing tautology . . . that only those facts are scientific which can be reduced to terms of nerve cells" and the claim for psychoanalysis as the "exclusive way to salvation" (Meyer, 1956).

In defending my thesis, I will develop two lines of argument: the first based on the recent history of psychiatry in the United States, the second on models of mind implicit in the way clinical problems are defined and managed. If an excursion into history needs justification, I remind you of Kanner's sage advice (1955) that just as "a careful anamnesis . . . is indispensable for an adequate understanding" of our patients, "an 'anamnesis of [our] specialty is an indispensible guide to the understanding of *its* present status."

Lineage of American Psychiatry

The lineage of our specialty began extramurally and thus was illegitimate by the canons of academe. Our forefathers[1] (like yours) were the superintendents of asylums for the insane—institutions situated at a considerable distance from centres of learning, and lacking a tradition of research. In 1894, at their 50th annual meeting, American asylum psychiatrists were castigated by a distinguished neurologist, Professor S. Weir Mitchell[2] of the University of Pennsylvania, the oldest medical school in your former colony (Mitchell, 1894): "Want of component original work is to my mind the worst symptom of torpor the asylums now present. . . Where . . . are your careful scientific reports?. . . You live alone, uncriticized, unquestioned, out of the healthy conflicts and honest rivalries which keep us (neurologists) up to the mark of the fullest possible competence. . ."

Within two decades of that withering criticism, the foundations for a research enterprise in psychiatry were laid at the New York Pathological Institute (1896), the Psychopathic Hospitals in Ann Arbor (1906) and Boston (1912), and the Henry Phipps Psychiatric Clinic (1913) in Baltimore (Whitehorn, 1944). However, those institutions remained no more than widely spaced oases in an academic desert; as late as 1958 (Appel & Pearson, 1959), most US medical schools had at best a part-time psychiatric faculty, heavily dependent on private practice, constantly hectored, and regarded as barely discriminable from its clientele.

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*The Eli Lilly Lecture, Winter Quarterly Meeting, Royal College of Psychiatrists, London, 21 January, 1986.

[1] *The American Journal of Psychiatry* began in 1844 as the American Journal of Insanity, edited by Amariah Brigham, Superintendent of the New York State Lunatic Asylum in Utica, just as the *British Journal of Psychiatry* began in 1853 as the *Asylum Journal* (later the Journal of Mental Science), edited by John Charles Bucknill, Superintendent of the Devon Asylum.

[2] Mitchell, along with other distinguished neurologists of the day, had taken the lead in criticising patient care in the asylums and in questioning the competence of their superintendents. They contended that, because insanity was a physical disease of the brain, the neurologist, with his scientific knowledge of CNS physiology and pathology, was best fitted for its treatment. The asylum psychiatrists rejoined that this unwarranted attempt to discredit them and their hospitals was motivated by a pecuniary interest in diverting mental patients to the private offices of the neurologists (Deutsch, 1944). The drama was played out during the trial of Charles Guiteau, who assassinated James Garfield, the President of the United States, on July 2, 1881. Neurologists, summoned by the defence, testified that Guiteau was insane, psychiatrists, summoned by the prosecution, that he was not (Rosenberg, 1968). In the event, the jury found Guiteau guilty, but the autopsy findings after his execution—at best equivocal—were hailed by the neurologists as vindicating their judgement.

If asylum psychiatry be taken as its sire, American psychiatry has psychoanalysis for its dam. Like the alienist, the psychoanalyst thrived outside the academy. Psychoanalytical training took place in extra-mural institutes, no less isolated than the asylums for sceptical criticism and equally unencumbered by scientific methodology. Here and there, departments of psychiatry and analytical institutes entered into liaisons; most have since been terminated on grounds of mutual incompatibility. Thus, our developmental history is an anomaly among medical specialties, in that influences outside academe had so powerful a role in determining its intellectual content and career lines.

When Psychoanalysis was in Vogue

The ascendancy of psychoanalysis in academic psychiatry in the post-War period was a peculiarly American phenomenon. In comparing the British and American scenes, Professor Lewis noted in 1953 that: "... none of the recognized teachers of psychiatry in the undergraduate medical schools of London is a member of the Psychoanalytical Society" (Lewis, 1953).

Professor Michael Shepherd (1957), in a paper written in the same era, contrasted the British scene, where the concepts of psychoanalysis were "transmitted through a semi-permeable membrane of critical examination and testing" with the American, where "a remarkable attempt [had] been made in many centres to ingest the whole system, python-like, into the body of academic opinion." By the early 1960s, more than half the chairmen of departments of psychiatry in the US held membership in analytical societies (APA Newsletter, 1962).

At that time, I fired off a salvo which sank without a trace: "From any scientific vantage-point, what is remarkable is the preoccupation with intensive individual psychotherapy. After some five decades of its advocacy as the preferred method for the treatment of emotional disorders, ... we have no evidence that any one way of doing it is better than any other or that long-term is superior to brief psychotherapy (Frank, 1961). Confronted with this distressing state of affairs, some ... reply that psychoanalysis was never really intended as a method of treatment but as a research tool for the investigation of the personality. But this is hardly any more credible, since the 'research' method seems to follow none of the accepted scientific principles of prediction, design, control, and quantification... The history of science ... is replete with instances in which an initially liberating conceptualization, once institionalized, becomes a barrier to progress" (Eisenberg, 1962).

That point of view was absent from the 1952 APA Conference on Psychiatric Education (Whitehorn, 1953). When I expressed it a decade later, at the final plenary session of the 1962 Conference, there was a veritable stampede of Department Chairmen to the floor microphones. (There were no Chairwomen, then. Of the 114 individuals listed as participants, only four were women. 0 tempora, 0 mores!) Just about every eminent figure present rose to defend the primacy of psychoanalysis as the 'basic science' of psychiatry; not one supported my critique in the public forum. My remarks, condensed to five sentences, appeared as a 'dissenting view' in the final publication (Barton & Malamud, 1963). However, by the 1976 Conference (Rosenfeld, 1976), "de-emphasis on a psychoanalytic orientation" was listed first among the shifts in professional training goals which had occurred over the prior decade.

Today, a very few departments excepted, neither asylum psychiatrists nor psychoanalysts are any longer heavyweights in academic psychiatry; the former were never fully incorporated, and their power base has shrunk with the decline in state hospital beds; the latter have been out-gunned by nosologists and neurobiologists in an era of scientific research. If this be progress for one dimension of psychiatry, it also embodies a very considerable hazard to another. To indicate why this is so, it is necessary to consider the developments in psychiatry in the context of the recent history of medicine as an applied science.

The Scientific Context of Practice

Although research in the natural and biological sciences began to exert a shaping influence on medical theory in the latter half of the 19th century, the biomedical model of disease did not have a major impact on clinical practice until the decades after World War II (Eisenberg, 1977a). The accelerating productivity of medical research and the growth of sub-specialisation in response to its discoveries resulted in a gradual narrowing of medical vision to the biological mechanisms of disease (Eisenberg, 1970). To ascribe this process to the perversity or insensitivity of physicians is to mistake consequence for cause. Precisely because specialisation resulted from, as well as contributed to, greater therapeutic power, it came to dominate professional ideology in medicine and surgery.

If the developmental course of general medicine identifies the origin of the methodological biases in its practices, the evolution of psychiatry clarifies the paradigms and procedures we have employed until quite recently. During the post-War years, when clinical psychiatry in the United States enjoyed a considerable expansion in faculty representation, in time in the medical curriculum, and in recruits to its ranks (Webster, 1969), its methods were primarily psychological; its departments were staffed by clinicians; training emphasised the meaning of the present illness in the context of the patient's past and the therapeutic use of the doctor-patient relationship. Psychiatry became particularly attractive to the clinically orientated medical student, who found it one of the few specialties with a persisting concern for the patient as a person in the era of organ-orientated medicine (Funkenstein, 1976). General practice, which might have provided an alternative, had almost ceased to enlist further recruits in the US because of its low prestige, difficult working conditions, and isolation from the medical mainstream.

How is it that psychiatry continued to preserve a central interest in the individuality of the patient, in an era when the other specialties lost sight of it? Were we inherently more compassionate or humane than our colleagues? It would be flattering to believe that to be true. The reasons were more prosaic; they are to be found in the state of our art.

At the turn of the century, two exciting and contradictory developments each promised to clarify the nature of mental disorders. On the one hand, the brilliant successes of bacteriology and pathology in unravelling the hidden core of general paresis appeared to presage similar discoveries for the other psychoses; on the other, psychoanalysis uncovered meaning in mental symptoms, and proposed that they were best understood as the result of deviations in development. When dementia praecox and manic depressive psychosis remained impervious to laboratory investigation, progressive disenchantment led to a virtual abandonment of the search for brain pathology. Depth psychology, though it abjured a role in the treatment of psychoses, opened a way to the ambulatory care of neurotic patients. Diagnosis and classification—the hallmarks of the medical approach—became almost irrelevant to clinical practice; analytically orientated psychotherapy dealt with constellations of individual and family dynamics, rather than with syndromes or diseases.

In effect, psychiatry made a virtue of the failure of biomedical science to discover effective means for the diagnosis and treatment of psychiatric disorders. If internists learned to focus on organ pathophysiology because it provided the basis for designing specific remedies, we psychiatrists continued to listen to our patients and to study their social interactions, because that alone enabled us to diminish suffering. The ideologies of both specialties had been determined pragmatically. And now the paradox emerges. Just at the moment when the rest of medicine is being pressed to expand its horizons to include the psycho-social determinants of illness, findings from therapeutic and basic research are sweeping psychiatry into the biomedical mainstream. These developments carry with them both the promise of far greater potency and the peril of the reification of disease that has characterised the other medical specialties.

Recent Occupational History

In the late 1940s and early 1950s, treatment of the psychoses was radically changed by a series of chance discoveries (Eisenberg, 1973): of reserpine's psychotropic effects when it was used to treat hypertension; of chlorpromazine as a 'tranquilliser' during research on anaesthesia; of iproniazid as a euphoriant when it was used to treat tuberculosis; of the antidepressant properties of imipramine during therapeutic trials for its expected neuroleptic effects; and of the anti-manic effects of lithium when Cade (1949) observed sedation in guinea pigs given uric acid as its lithium salt, chosen solely because of its solubility. The serendipity of these findings does not deprecate them, but it emphasises the lack of coherent biological theories to guide their discovery; those theories emerged in the effort to account for what had been observed.

The new therapeutic armamentarium has had major consequences for the practice of our specialty. It provided the means for aborting acute psychotic episodes and for minimising recurrences. Because remissions could be induced in a relatively short time-frame (and because insurance coverage became available), psychiatric units in American general hospitals expanded rapidly (Taube & Barrett, 1983). Because the new agents were relatively syndrome-specific, diagnosis and classification, which had previously concerned few American psychiatrists outside of Washington University at St. Louis (Klerman, 1982), now became important clinical issues for effective patient care, and paved the way for DSM III. Not the least of the benefits of psychopharmacology has been the development of methodologies for the double-blind evaluation of new therapeutic agents, whether they be drugs, social interventions, or psychotherapies (Klerman, 1974).

However, by far the most important result of the discovery of psychoactive drugs was the stimulus it provided for research in neurobiology. The scientific yield has been extraordinary! Forty years ago, norepinephrine and acetylcholine were the only chemicals believed to act at the synapse; their receptors had not yet been identified, and the brain was viewed as an electrical switchboard, with its connections precisely wired according to genetic instructions. Today, candidate neurotransmitters number 60, and we are still counting; more than 25 specific receptors at cell surfaces have been identified (Snyder, 1984; Richardson *et al,* 1985). The acetylcholine-gated sodium channel has been characterised in exquisite detail; it is a transmembranous protein consisting of five sub-units, the genes for each of which have been specified (Mishina *et al,* 1984, 1985a) and the electrical properties of which have been determined (Mishina, 1985b). We now know of neuromodulators—intercellular chemical messengers which produce relatively enduring changes in the responsiveness of synaptic elements (Stanfield *et al,* 1985; Aghajanian, 1985; Ewald *et al,* 1985); they appear to act by altering the properties of ion channels. In effect, the brain modifies its own responsiveness to incoming stimuli (Stevens, 1985).

The plasticity of brain structure has been highlighted by the discovery of competition between axon terminals, which proliferate in excess early in development, and of feed-forward and feed-backward between pre- and post-synaptic cells; the pattern of functional activity shapes and reshapes synaptic architecture (East *et al,* 1985). Because cell adhesion is a pivotal step in neuroembryology, the discovery of nerve cell adhesion molecules (N-cams), the cloning of their genes, and the recognition of changes in the composition of N-cams during development has made it possible to study what determines the hard-wiring of the brain (Edelman, 1984; Cunningham, 1985). It is now possible to examine the molecular concomitants of learning and to distinguish the chemical events underlying short-term versus long-term memory in simpler organisms (Kandel, 1985). The more we learn about the neurobiology of the brain (Kandel & Schwartz, 1985), the more we appreciate the complex interactions between its components (Bloom, 1984; Synder & Reynolds, 1985), the less tenable is a purely internalist account of its functions, as Changeux (1985) has emphasised.

All of this has had an exhilarating effect on psychiatric research, but in what sense does this enormous promise also embody a peril? The peril is that psychiatry may come to focus exclusively on the brain as an organ and to overlook the experience of the patient as a person. We have been for so long pilloried by our medical and surgical colleagues as witch doctors and woolly-minded thinkers that it is tempting to seek professional respectability by adhering to a reductionistic model of mental disorder. We may trade the one-sidedness of the 'brainless' psychiatry of the past for that of a 'mindless' psychiatry of the future.[3] Today, even psychoanalysts find it convenient to recall that Freud (1914), himself a product of 19th century reductionism, cautioned his followers that: "All our provisional ideas will some day be based on an organic substructure... We take this possibility into account when we substitute special forces in the mind for special chemical substances."

A Parable for our Time

Let me set the danger forth, plain for all to see, by citing research undertaken in my own Laboratory of Mental Science. The starting point for our studies was the neurobiological breakthrough by Rene Descartes (1649), identifying the pineal as the seat of the soul.[4] In his words: "The part of the body in which the soul exercises its functions immediately is in nowise the heart, nor the whole of the brain, but merely the most inward of all its parts, to wit, a certain very small gland which is situated in the middle of its substance and so suspended above the duct whereby the animal spirits in its anterior cavities have communication with those in its posterior, that the slightest movements which take place in it may alter very greatly the course of these spirits; and reciprocally that the smallest changes which occur in the course of the spirits may do much to change the movements of this gland... The whole action of the soul consists of this, that solely because it desires something, it causes the little gland with which it is closely united to move in the way requisite to produce the effect which relates to this desire."

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[3] I first heard this contrast employed by Professor Ernest M. Gruenberg of the Johns Hopkins University; he in turn credits it to the late Professor Herbert G. Birch of the Albert Einstein College of Medicine. It had, of course, its predecessors, one of which may merit mention. Some 70 years ago, Elmer E. Southard, first Director of the Boston Psychopathic Hospital and Bullard Professor of Neuropathology at Harvard Medical School, condemned theories which ascribed mental disorders *either* to "blots and spots in the brain" *or* "tangles and twists in the mind". He regarded as "pernicious... the doctrine which proposes to separate mind and body before we know much about either" (Southard, 1912).

[4] Herophilus of Alexandria (4th century B.C.) is said to have proposed that the pineal, because of its location, served as a tap to regulate the flow of thought *(pneuma psychikon)* from the third to the fourth ventricle. Galen (2nd century A.D.) rejected this hypothesis because he noted that the pineal is situated outside of the ventricular system (Kappers, 1979). In any event, Herophilus cannot properly be granted priority of publication because none of his writings survive except in secondary sources!

Accordingly, our research team grew pineal cells in tissue culture and eluted from the supernatant an unique protein. Against this pineal-specific protein, we prepared a monoclonal antibody which had been made radioactive by incubating the hybridoma cells with ^{15}O labelled acetate. Administered parenterally, the tracer molecule, modified to permeate the blood-brain barrier in the region of the pineal body, binds to the gland tightly and specifically. As the positrons emitted by ^{15}O collide with electrons in the adjacent tissues, the gamma rays produced by particle annihilation are detected and converted by appropriate instrumentation into a visual image. A major step forward occurred when our engineers succeeded in constructing a luminescent screen on which moment-to-moment changes can be displayed. Thus, displacements in the pineal (accompanied, as Descartes had predicted, by ventricular currents) can be correlated with fluctuations in the state of the soul. A final refinement was to freeze-dry the antibody, permitting it to be sniffed into the nasal cavity, thus avoiding the necessity for venapuncture by those psychiatrists who can't stand the sight of blood. Our marketing consultant chose the name *PinealPet®* for the instrument, in tribute to its now antiquated predecessor, the Positron Emission Tomograph (Phelps & Mazziota, 1985).

That must suffice for an account of the science of the matter. Now consider its economics. *PinealPet* can be guaranteed to increase the earning capacity of American psychiatrists handsomely, when they work in a fee-for-service system. Because its immediate imaging properties make it ideal for office use, psychiatrists rather than radiologists can bill for it, and thus attain economic parity with other technology-based disciplines. Because it will no longer be necessary to inquire of the patient about the state of his or her soul, a notoriously time-consuming, uncertain and altogether messy procedure, time savings will be prodigious; productivity will increase; its cost-effectiveness will please both supply side and free market economists. For myself, I intend to ask no profit (other than the tax-free Nobel Prize money).

Furthermore, the therapeutic potential of this technological advance will not have escaped you. It should prove possible, in principle, by a kind of psychochiropractic, to correct the subluxations of the pineal which result in existential *angst*. By means of the piezoelectric effect, the therapist should be able to manipulate the pineal body with pulses of current under direct visual control to align it in such fashion as to produce harmony in the soul.

Yet, at the very point that the device was ready to be marketed, I was afflicted by an acute crisis of conscience, in all probability resulting from *mal de mer* of the pineal. I melted the instrument down; I shredded blueprints and protocols before they could be copied by sinister commercial interests. In the nick of time, I had realised the consequences of my thought experiment.

Once at hand, *PinealPet*, like the endoscope and the cardiac catheter before it, would have come to dominate clinical practice through its potential for increasing earnings *and* its capacity to generate nominally objective data. A technology invested with the authority of science is irresistible to patient and doctor alike in reifying disease.

Sermon on the Parable

Despite the hyperbole, I intend this thought-experiment and the scenario of its consequences as a serious parable for the impact of the new biotechnology on the way psychiatrists work and how they think about their work. How far does it apply? Consider, first, some aspects of current practice and next, their implications for models of the mind.

Recently, the mail brought me an unsolicited copy of *PDLA Biopsychometry* (1985), an advertisement in the guise of a journal, which claims to "place science at the service of the physician" by providing "the most sophisticated neurochemical and biochemical analyses available ..." including "gas chromatography/mass spectroscopy, high performance liquid and gas chromatography, plasma emission spectroscopy, dopamine receptor assays and computer analysis of therapeutic drug levels." Among the tests touted to the practitioner is the dexamethasone suppression test (DST); yet an expert review of the evidence at an NIMH Workshop in July, 1982 highlighted problems with sensitivity and specificity, failure to predict treatment responsiveness, and false positives produced by concurrent medical conditions or medication; the panel concluded that: "the DST is a useful research tool, but at this time there are *no* clear indications for its *routine* use in the diagnosis or clinical management of depression" (Hirschfeld *et al*, 1983).

Data reported since the 1982 workshop provide further evidence that inadequate specificity and sensitivity continue to limit the utility of the DST as an adjunct to diagnosis or prognosis (Hudson *et al*, 1984; Stokes *et al*, 1984; Arana *et al*, 1985; Avery *et al*, 1985; Brown *et al*, 1985). Much the same can be said for the clinical use of a number of other biological assays for psychiatric patients: TRH (thyroid releasing hormone), TSH (thyroid stimulating hormone), VMA (vanillyl mandelic acid), MHPG (3-methoxy, 4-hydroxy phenylglycol), and HIAA (5-hydroxy indolacetic acid); "rather than their being established laboratory aids... their promise remains to be fulfilled" (Rubin, 1985). As to X-ray computed axial tomography (CAT) scans, Weinberger (1984), in a comprehensive review, acknowledged their value for the differential diagnosis of neurological lesions, but concluded: "CAT scan findings associated with chronic schizophrenia ... are not consistent enough to have diagnostic or prognostic implications in individual cases."

Then, what accounts for the increasing use of these procedures by clinicians? Their potential for generating income for ancillary charges has obvious appeal to hospitals and to commercial laboratories. However, with the exception of those clinicians with a direct stake as investors in such ventures, itself a violation of the relationship of trust between doctor and patient (Relman, 1980), testing brings no financial benefit to the practitioner. Nonetheless, market forces may be contributing to the new craze for biomedical tests. Increasing competition from non-medical mental health 'providers' for third-party reimbursement in the United States has prompted us to run our medical credentials up the flagpole. Lacking credible evidence that psychotherapeutic efficacy correlates with the discipline of the therapist, we have found it politic to emphasise our medical skills for differential diagnosis and somatic treatments. I do not imply that these claims are without foundation or relevance, but it *is* disconcerting that they have been rediscovered only in the context of protectionism. Is it possible that ordering tests before they have been validated bespeaks, not only an inability to assess the evidence, but also a rush to biomedical camouflage? More than that, it implies a belief that 'objective' biological measures are *ipso facto* more reliable than clinical assessment, and that psychiatry is 'scientific' to the degree it subscribes to the "neurologizing tautology" (Meyer, 1912).

In my *PinealPet* scenario, the device was designed as an office procedure to be billed for by the psychiatrist-operator, and this led to the prediction that it would come to dominate clinical practice because of the financial incentive built into it. There is no reason to believe that psychiatrists, if our discipline comes to have a reimbursable technology base, will be any more able than other specialists in a fee-for-service system to resist procedures that are always good for the doctor and sometimes good for the patient. The hourly earnings of the gastroenterologist are more than six times greater from the use of the endoscope than from providing general clinical care (Almy, 1981); this disproportion threatens to transform gastroenterologists into mere endoscopists[5] (Spiro, 1974). Before you dismiss this as an American disease against which you are immunised by the National Health Service (even as Mrs Thatcher is proceeding to dismantle it), note that Clark (1985) has already detected early warning signs among endoscopists in the UK.

To ascribe this phenomenon to cupidity on the part of physicians is unjust; that is true for only a few. Over-use results from: gradual broadening of indications for a test as it becomes part of a 'complete workup'; wanting to be 'certain' all possible disease has been ruled out (in part to avoid a malpractice suit for a case missed); and pressure to justify the catheter suite to administrators when appropriate referrals lag, as diagnostic centres multiply beyond need. Under-employed doctors (increasing in numbers in both our countries) who come bearing technology endanger the public health.

My thought experiment incorporated a second key premise: that brain structure and mind (soul) are isomorphic. Expressed as a biochemical metaphor, that belief inheres in the statement: for every twisted thought, there is a twisted molecule. In that aphorism, as in my parable, the vector of causality is unidirectional: *from* brain *to* mind. In consequence, diagnosis is directed at identifying the brain pathology, treatment at correcting it. Descartes granted soul its own sphere of action, but ceded it to the church; in return, he claimed the body for physiology; in contemporary Cartesianiasm, priests have been replaced by secular counsellors. Thus, Szasz (1960) insists on a distinction between "diseases of the brain which are problems for neurology" and "problems in living" which are the proper domain of psychiatry. Twenty-five years later, Szasz (1985) continues to adhere to this position, when he refers to "the pervasive ambiguity that has always shrouded the subject matter of psychiatry. Is psychiatry's domain mental illness, a term most psychiatrists contend denotes a proven or putative brain disease? Or is it the study of interpersonal processess....?" To conflate the one with the other under the single rubric of mental illness is, in his words, to create: "a myth ... to disguise the bitter pill of moral conflicts in human relations".

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[5] A 'psychic endoscope' may be on its way. While I was at work on *PinealPet*, Dr Francois M. Mai was kind enough to call to my attention his own experiments with a laser-based 'psychoscope', which "enables ego, superego and id" to be visualised and differentiated one from another (Mai, 1983).

However attractive this dichotomy may be to a psychiatrist who limits his practice to voluntary (and well-heeled) patients 'suitable' for intensive psychotherapy, it is belied by the actual patterns of illness in the community. Diseases of the brain and problems of living are overlapping categories, not either-or. Brain disease makes problems in living more rather than less likely (Rutter, 1981); yet brain pathology does not in itself account for all the patient's problems, at least until it is so extensive that personhood has all but disappeared (Eisenberg, 1977b). Moreover, patients with symptoms resulting from problems in living—who make up a third to a half of those who consult primary care doctors—have no less legitimate claims to care than do those with identifiable organ pathology (Eisenberg, 1977c). Indeed, problems in living necessarily influence brain state and structure—unless, of course, one believes that mind floats about in an incorporeal ectoplasm. Recent research on psychiatric disorders as different as depression, panic disorder, and schizophrenia exemplifies the ubiquity of brain/mind interactions.

Brain Diseases or Problems in Living?

The work of George Brown (1978) provides substantial documentation for the role of stressful life events in precipitating episodes of depression. At the same time, there is considerable evidence that biochemical derangements, including reduced sensitivity of beta-adrenergic receptors on the lymphocytes of patients with agitated depression (Mann *et al*, 1985), often accompany depression (Davis, 1983); familial aggregation argues strongly for genetic transmission of susceptibility (Berretini *et al*, 1984). There is by now extensive documentation that electroconvulsive therapy (NIH Consensus Conference, 1985), tricyclics, and MAO inhibitors relieve the symptoms of depression and that lithium and tricyclics minimise recurrence (NIH Consensus Conference, 1984), although it is noteworthy that every randomised controlled trial reveals a sizable but variable group of patients who remit while on placebo, as well as others who respond to neither. Beck *et al* (1979, 1985) have shown that cognitive therapy leads to rates of improvement as substantial as those produced by drug therapy, whereas adding a tricyclic to cognitive therapy does not add to the benefit. To complicate the matter, George Murphy and his colleagues (1984), having confirmed Beck's findings, have also shown that the psychological traits of depressed patients which cognitive therapy was specifically designed to alter are modified equally well by drugs (Simons *et al*, 1984). On the other hand, Weissman *et al* (1981) report that, although the symptoms of depression are relieved more effectively by drugs, the patient's interpersonal difficulties respond better when concomitant psychotherapy is provided. Thus, if empirical evidence makes a difference, one would have to conclude that depressed patients exhibit problems of mind *and* brain, and that changes in the one alter the other.

I turn now to panic disorder. During the first half of my career, there was hardly a hint in the literature that panic attacks were other than purely psychological events, and the explanations for them either psychodynamic or based on learning theory. When Pitts & McClure (1967) first reported that intravenous lactate precipitated panic episodes in patients (at a much higher rate than in controls), the finding was largely ignored; it has now been replicated with sufficient frequency to have become part of common knowledge. Soon, we learned that 'antidepressant' drugs could produce a remission of symptoms (Klein & Rabkin, 1981); more remarkably, successfully treated patients no longer respond to lactate infusion with panic (Rifkin *et al*, 1981). Charney *et al* (1984; 1985) have demonstrated greater sensitivity both to yohimbine, an alpha$_2$-adrenergic receptor antagonist, and to caffeine, an adenosine receptor antagonist, in patients with panic disorder, when compared to normal controls. Further, Reiman *et al* (1984), in a comparison of cerebral blood flow (CBF) between eight lactate-responsive panic disorder patients and 25 normal controls, demonstrated a significant asymmetry of CBF in a region of the parahippocampal gyrus. Despite this array of findings, it remains the case that behaviour therapy is effective for many such patients (Gelder *et al*, 1967), although the specificity of its effects in comparison to other psychological treatments has been challenged (Klein *et al*, 1983). Other investigators (Bonn *et al*, 1984) have reported success in obtaining symptom relief by retraining breathing patterns. Thus, we confront a disorder manifested entirely in behavioural terms and amenable to various forms of psychotherapy—a 'problem in living' if you will; yet, at the same time, it is characterised by lactate sensitivity, an asymmetry in parahippocampal blood flow, and responsiveness to pharmacology—a 'brain disease', if you insist.

To many of our colleagues, the evidence that the schizophrenias are heterogeneous brain diseases is becoming ever more persuasive because of the evidence for familial inheritance (Gottesman & Shields, 1982; McGuffin, 1984); abnormalities in neurochemistry (Snyder, 1982), cerebral circulation (Gur *et al*, 1983, 1985), cerebral metabolism

(Buchsbaum *et al*, 1982; Ariel *et al*, 1983; Wolkin, *et al*, 1985); and structural defects in brain (Weinberger *et al*, 1983; Boronow *et al*, 1985; Owens *et al*, 1985; Reveley, 1985). Equally noteworthy is the occurrence of otherwise unexplainable motor disorders in patients with severe psychiatric disease—disorders which antecede the modern introduction of neuroleptics, though they have become more prominent since their use (Rogers, 1985). These abnormalities are present, it is true, only in some patients and completely absent in others, but remain persuasive in the aggregate.

Nonetheless, the trajectory of the schizophrenic illness remains exquisitely sensitive to both macro and micro cultural differences. In the World Health Organisation (1979) nine-country study, patients at each of the participating national centres were diagnosed as schizophrenic by common criteria. Yet, at the two-year follow-up, there were substantial differences in clinical outcome, with patients in developing countries (Nigeria, India, Colombia) exhibiting a more favourable course than patients in the industrial world (US, Czechoslovakia, UK, and Denmark). However, apparent differences may, in part, reflect sampling errors and differences in premorbid factors. Indeed, only recently have substantial data on the outcome of a representative sample of schizophrenic patients (diagnosed by PSE criteria) become available. Watt *et al* (1983) have reported a five-year follow-up on all such patients admitted from a defined catchment area of a half million persons, during a 20-month period. The percentage with a good outcome, just under half the total sample, was higher than might have been expected. However, comparable data from the developing world are not obtainable, so that final assessment of the WHO findings must remain in abeyance.

As to microcultural factors, Brown *et al* (1962, 1972) have shown that the likelihood of relapse in schizophrenic patients discharged from hospital is significantly greater among patients returning to families exhibiting high 'expressed emotion' (Vaughn & Leff, 1976a). The number of hours of face-to-face contact between the patient and family is decisive; if it is less than 35 hours a week, the likelihood of relapse is half as great (Vaughn & Leff, 1976b; Vaughn *et al*, 1984). Phenothiazines protect patients in hostile families against relapse, but they offer less benefit to those in more accepting homes—another instance of drug/environment interaction (Leff *et al*, 1982, 1983). When family treatment succeeds in lowering 'expressed emotion' in high-risk families, the relapse rate of patients declines in parallel (Leff *et al*, 1985). Randomised controlled trials in the US have shown that psycho-social interventions directed at patients (Hogarty *et al*, 1973) and at families (Falloon *et al*, 1982, 1985) augment the power of neuroleptics to enable chronic schizophrenic patients to maintain themselves in the community (Barrowclough & Tarrier, 1984). Once again, the 'problems in living' which accompany presumptive brain disease prove to be responsive to social interventions, no less than to medication, and to be managed best by combinations of both.

Conclusion

An analogy more suggestive than precise is that exclusively biological and psychological theories in psychiatry stand in relation to one another much as wave and particle theory do in subatomic physics. However attractive this metaphor for the mind-brain inter-relationship, it must be emphasised that it does not extend to the deeper meaning of the Bohr principle; namely, that "the finite interaction between object and measuring agencies conditioned by the very existence of the quantum of action entails . . . the necessity of a final renunciation of the classical ideal of causality and a radical revision of our attitude toward the problem of physical reality" (Bohr, 1949).[6]

Under one set of experimental conditions, the phenomena observed (interference patterns) are explicable only by wave theory; under another set, the phenomena (spontaneous and induced emission of radiation) are explicable only by quantized particles. Despite the apparent contradiction (i.e., that photons and electrons are simultaneously waves *and* particles), both formulations are necessary to account for the universe of observation. The resolution of the 'contradiction' lies in the recognition that: "The spatial continuity of our picture of light propagation and the atomicity of the light effects are complementary aspects in the sense that they account for equally important features of the light phenomena which can never be brought into direct contradiction with one another, since their closer analysis in mechanical terms demands mutually exclusive experimental arrangements" (Bohr, 1932).

This 'complementarity principle' characterises all attempts to explicate medical conditions: the demonstrable pathology of disease does not suffice to explain the very considerable variance in the illness experience which accompanies apparently identical lesions (Eisenberg, 1970). The quality and duration of the illness experience are shaped by a sick role constructed out of cultural beliefs, by the patient's niche in family and social structure, and out of psychological traits idiosyncratic to the patient, no less than by organ pathology.

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[6] Indeed, Bohr himself made an excursion into biology in 1932 which led him to emphasise "the impossibility of a physical or chemical explanation of the peculiar function characteristics of life" (Bohr, 1932)—a conclusion he rejected 30 years later when he recognised that "the task of biology cannot be that of accounting for the fate of each of the innumerable atoms permanently or temporarily included in a living organism" (Bohr, 1962).

There is not now, nor can there be, a technical device capable of transducing brain structure or chemistry into social meaning. As Kety (1960) pointed out: "It requires just as much oxygen to think an irrational thought as to think a rational one." To be sure, information (in the sense of order as opposed to randomness) inheres in neural connectivity and molecular configurations. Meaning presupposes ordered working of the cerebral machinery, but it is a property that emerges only in a human social context. Those who search for mind in the machine will find at the end of their journey what Gertrude Stein said about her trip to a nondescript town: "When you get there, you find there's no *there* there!"

What brings patients to doctors is discomfort and dysfunction, not the pathology which may underlie them (Eisenberg, 1980). It matters—and matters greatly—to strategies for cure just how far bodily malfunction is causing problems in living and how far the symptoms are the somatic embodiment of problems in living; rarely are they simply one or the other. The doctor's task is to identify their sources when this can be done, to reach agreement with the patient about their significance, to indicate the range of available remedies, and to assist the patient in coping with what is beyond repair. In this process, biomedical knowledge is necessary but not sufficient; the doctor's transactions with the patient must be informed by the social sciences.

Neither brainlessness nor mindlessness can be tolerated in psychiatry or medicine. The unique role of psychiatry in medicine will be found in the extent to which it contributes to the understanding of psychosomatic and somatopsychic integration; i.e., to the ways in which the mind is embodied and the body literally mindful (Hahn & Kleinman, 1983).

The task is daunting. We have no equivalent of the Lorentz transformation equations to enable us to account for the disparities between inertial frames of reference. Yet, however far from our goal we may be, the very striving for it is the *raison d'être* of our specialty. That is what makes psychiatry such a heady enterprise!

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Leon Eisenberg, MD, *Professor of Psychiatry and Professor and Chairman, Department of Social Medicine and Health Policy, Harvard Medical School, Boston, Massachusetts 02115, USA.*

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Deficits of Chronic Schizophrenia in Relation to Long-Term Hospitalisation

P. JOHN MATHAI and P. S. GOPINATH

Eighty chronic schizophrenic and 16 manic-depressive psychotic patients conforming to Research Diagnostic Criteria were examined in terms of their mental state, cognitive functioning, current behaviour, and neurological status. They comprised out-patients, day-care patients, and long-stay in-patients belonging to two mental hospitals with different social conditions. Assessed deficits were not significantly related to record variables such as age, duration of illness, duration of hospitalisation, or treatment received. Analysis of the different groups of patients reveals that long-term hospital care has had little effect on the deficits of chronic schizophrenia, and suggests that these are integral features of the disease process.

The hypothesis that the deficits of chronic schizophrenia are due to the disease process, and are not attributable to external factors such as hospital care (Johnstone *et al*, 1981) provokes a renaissance of interest in these deficits. This hypothesis tends to complicate the hitherto inviolate (and ingenious) concept of institutionalisation. Further studies are warranted to renounce or renovate that concept, and to understand the respective contributions of biological process, hospital care, and treatment received to the development of the "defect state" in patients with chronic schizophrenia.

A review of the literature reveals a consonance of opinions regarding the existence and nature of deficits in chronic schizophrenia (Kraepelin, 1919; Wing & Brown, 1970; Bhaskaran et al, 1972; Crow, 1980; Owens & Johnstone, 1980; Johnstone *et al*, 1981; Andraesen, 1982; Maser & Keith, 1983; Weinberger *et al*, 1983; Taylor & Abrams, 1984), but evidence concerning their causes has been accumulated under different headings, such as a social hypothesis (Wing & Brown, 1961), a disease process hypothesis (Johnstone *et al*, 1981), and an alternative hypothesis (Marsden, 1976).

The present investigators have attempted to study the deficits of chronic schizophrenia, in the light of these mutually contradictory hypotheses, and to consider whether they are in fact integral features of the schizophrenic process or consequences of long-term hospital care, by comparing:

1. The deficits of long-stay-in-patients with chronic schizophrenia and with manic-depressive psychosis in the same hospital.
2. The deficits of long-stay chronic schizophrenic patients in two mental hospitals with different social structures and staff patterns.
3. The deficits of long-stay patients, day-care patients and outpatients with chronic schizophrenia.

Method

This study was conducted at two mental hospitals in south India. The one at Bangalore is the clinical psychiatric wing of the National Institute of Mental Health and Neuro Sciences (NIMHANS). This is a service, teaching, and research hospital, where as well as psychiatrists, clinical psychologists, psychiatric social workers, and psychiatric nurses are trained. The other mental hospital (MH) is a non-teaching, non-academic, service-oriented institution. The two hospitals differ markedly in their social conditions, staffing patterns and administrative policies. They score respectively 61 points and 7 points on Barton's proposed scale for rating psychiatric hospitals (Barton, 1965).

Sample

The sample consisted of 96 male and female patients, between the ages of 20 and 55 years, conforming to Research Diagnostic Criteria (Spitzer *et al*, 1978) for schizophrenia and manic-depressive psychosis. Specific exclusion criteria were epilepsy, organic mental disorders, alcohol dependence, drug dependence, mental retardation, major systemic debilitating physical illness like tuberculosis, diabetes and malignancy, and leucotomy and other neurosurgical procedures. It was subdivided into four groups of 20 chronic schizophrenic patients and one group of 16 patients with manic-depressive psychosis (affective illness). The first three groups were from NIMHANS and the latter two were from MH. "Long-Stay", in the present study, meant continuous hospitalisation for more than two years.

Group I: Long-stay chronic schizophrenic patients at NIMHANS who had had at least two years of continuous

TABLE I
Recorded variables

Recorded variables	*Group I n=20 Long-stay (NIMHANS)*		*Group II n=20 Day care (NIMHANS)*		*Group III n=20 O.P. (NIMHANS)*		*Group IV n=20 Long-stay (MH)*		*Group V n=16 Long-stay (MH) MDP*	
	Mean	*s.d.*	*Mean*	*s.d.*	*Mean*	*s.d.*	*Mean*	*s.d.*	*Mean*	*s.d.*
Age	42.35	9.3374	35.7	10.3877	40.15	7.8019	45.2	7.3097	39.81	9.435
Duration of illness (Yrs)	16.84	5.9490	12.279	6.5116	12.07	4.4428	20.075	7.0492	10.167	4.4197
Age of onset (Yrs)	25.15	7.8289	24.05	6.9792	28.15	4.4871	25.15	5.8604	29 25	8.5595
Total period of hospitalisation	13.9385	7.1999	2.913	2.4484	6.4183	0.3175	15.4665	7.5350	8.0043	4.3623
Total medication received (equivalent to chlorpromazine in Kgs.)	2.1315	1.9464	0.9515	0.4142	1.155	0.8306	1.275	0.2950	0.7612	0.6357
Medication during 1st 5 yrs (equivalent to chlorpromazine in Kgs.)	0.341	0.3399	0.2595	0.3448	0.358	0.4774	0.7269	0.3997	0.1519	0.0657
No. of ECTs	41.25	29.6157	31.6	20.0050	19.5	15.8592	70.05	45.8297	25.43	11.5121

TABLE II
The Nature of deficits

	I n=20 Long-stay (NIMHANS)		*II n=20 Day care (NIMHANS)*		*III n=20 O.P. (NIMHANS)*		*IV n=20 Long-stay (MH)*		*V n=16 Long-stay (MH) MDP*	
	Mean	*s.d.*	*Mean*	*s.d.*	*Mean*	*s.d.*	*Mean*	*s.d.*	*Mean*	*s.d.*
Positive symptoms	1.35	1.8100	0.45	0.5104	2.9	2.2219	0.8	1.3992	0.5	1.4142
Negative symptoms	55	28.3344	45.95	22.2367	59.35	19.7822	57.1	21.0835	2.3125	8.9868
*Mental state deficits	56.25	29.0460	46.35	22.2551	65.6	14.0202	60.15	35.6034	2.625	10.2364
Cognitive functioning	16.25	7.2756	21.7	5.8499	19.8	6.6495	13.5	4.6282	24.5625	2.9204
Current behaviour	8.6	3.9789	5.9	2.8457	8.80	3.7500	9.80	4.0859	1.31	1.9906
**Total deficits	78.35	38.7628	60.55	29.3803	84.6	21.6585	82.75	27.0416	6.375	2.9411

*Total of positive and negative symptoms.
**Mental state deficits + Cognitive impairment + Current behaviour

TABLE III
Relationship between recorded variables and deficits in chronic schizophrenic patients

Recorded variables	*Positive symptoms*	*Negative symptoms*	*Mental state deficits*	*Cognitive functioning*	*Current behaviour*	*Total deficits*
Age	0.0300	0.1194	−0.2913	−0.0699	0.0699	0.1586
Duration of illness	−0.1293	0.0400	−0.2260	0.0400	−0.0997	0.0200
Age of onset	−0.0300	0.0360	−0.2821	0.0699	0.0400	−0.1974
Total medication	−0.0599	0.0003	−0.1781	0.0200	−0.1293	−0.1586
Medication during first 5 years	0.2070	−0.0300	0.0997	0.1684	−0.2355	−0.1293
ECT	0.1684	0.0599	0.0100	0.0400	−0.0699	0.2355
Duration of Hospitalisation	−0.4132	0.2415	0.1871	0.0281	0.2342	0.3215

hospitalisation at the time of assessment and had never had long-stay or day care at any hospital other than NIMHANS.

Group II: Chronic schizophrenic patients living at home and receiving day care at NIMHANS, who had never had a long stay at any hospital during the entire course of their illness.

Group III: Chronic schizophrenic patients living at home and attending the out-patient department at NIMHANS, who had never had a long stay or day care at any hospital.

Group IV: Long-stay chronic schizophrenic patients at MH, who had completed at least two years of continuous hospitalisation at the time of assessment and had never had a long stay, or day care, at any other hospital.

Group V: Long-stay in-patients with a diagnosis of manic depressive psychosis (MDP) at MH, who had completed at least two years of continuous hospitalisation at the time of assessment and had never had a long stay, or day care, at any other hospital.

Assessment

Historical data and details of past treatment (recorded variables), which included age, sex, duration of illness, age of onset, duration of hospital care and physical treatment received by the patient, were collected systematically with the aid of a proforma compiled for the purpose. Mental state was assessed using a scale for rating chronic pyschotic patients (Krawiecka *et al*, 1977) and the Scale For Assessment of Negative Symptoms (SANS—Andreasen, 1981). We used the former to rate positive symptoms only and the latter to rate negative symptoms. The Mini Mental State

TABLE IV
Correlation between deficits in chronic schizophrenic patients

Deficits	*Positive symptoms*	*Negative symptoms*	*Cognitive functioning*	*Current behaviour*
Positive symptoms	—	0.1534	−0.1031	0.2152
Negative symptoms	0.1534	—	−0.7126	0.8105
Cognitive functioning	−0.1031	−0.7126	—	−0.6255
Current behaviour	0.2152	0.8105	−0.6255	—

TABLE V
Comparison between long-stay schizophrenic and manic depressive psychotic patients at MH with regard to deficits

Deficits	*Group IV, n = 20 Long-stay schizophrenic patients at MH*		*Group V, n = 16 Long-stay MDP patients at MH*		*Comparison and significance*
	Mean	*s.d.*	*Mean*	*s.d.*	
Positive symptoms	0.80	1.3992	0.50	1.4142	t = 0.6363 df = 34 NS
Negative symptoms	57.10	21.0835	2.3125	8.9868	t = 10.4911 df = 34* $P = <0.001$
Mental state deficits	60.15	35.6034	2.625	10.2364	$x^2 = 22.05$ df = 1 $P = <0.001$
Cognitive functioning	13.50	4.6282	24.5625	2.9204	t = 22.8140 df = 34 $P = <0.001$
Current behaviour	9.80	4.0859	1.31	1.9906	t = 7.6026 df = 34 $P = <0.001$
Total deficits	82.75	27.0416	6.375	2.9411	F = 210.0647 df = 1,33** $P = <0.001$

*Beheren's Fisher test.
**Age corrected analysis of covariance.

(MMS—Folstein *et al*, 1975) and the Ward Behaviour Scale (WBS—Wing & Brown, 1961) were used to rate cognitive impairment and current behaviour respectively. A detailed neurological examination was carried out on each patient and neurological deficits were recorded.

Procedure

In this investigation, the entire in-patient population (405) and the day care population (168) at NIMHANS, the entire in-patient population at MH (572) and the 462 patients who attended the out-patient department of one of the six adult psychiatry units at NIMHANS over a period of two months were surveyed. Thirty-six in-patients, 84 day care patients and 64 out-patients at NIMHANS and 104 in-patients at MH satisfied the specific criteria laid down for chronic schizophrenia in the study. Random samples each of 20 patients who satisfied all the criteria from among in-patients and the day-care patients at NIMHANS were assessed (Group I and II). A random sample of 20 patients who satisfied the criteria for the out-patient sample and who also had a duration of illness more than five years were assessed (Group III). A random sample of 20 chronic schizophrenic patients from MH, (matched for sex with group I) who satisfied the criteria were selected and assessed (Group IV). The sampling was done in all these instances using the table of random numbers.

All the 16 long-stay patients with a definite diagnosis of manic-depressive psychosis at MH were assessed (Group V). They were regular patients, admitted through the magistrates, whose recorded variables were obtained from the case sheets.

TABLE VI

Comparison between long-stay schizophrenic patients at NIMHANS and at MH with regard to deficits

Deficits	*Group I, $n = 20$ Long-stay (NIMHANS)*		*Group IV, $n = 20$ Long-stay (MH)*		*Comparison*	
	Mean	*s.d.*	*Mean*	*s.d.*		
Positive symptoms	1.35	1.8100	0.8	1.3992	$t = 1.0736$ $df = 38$	NS
Negative symptoms	55	28.3344	57.1	21.0835	$t = 0.2659$ $df = 38$	NS
Mental state deficits	56.25	29.0460	60.15	35.6034	$t = 0.0854$ $df = 38$	NS
Cognitive functioning	16.25	7.2756	13.5	4.6282	$t = 1.4263$ $df = 38$	NS
Current behaviour deficits	8.6	3.9789	9.80	4.0859	$t = 0.6273$ $df = 38$	NS
Total deficits	78.35	38.7628	82.75	27.0416	$t = 0.4163$ $df = 38$	NS

TABLE VII

Comparison between long-stay, day-care and out-patients at NIMHANS with regard to deficits

Deficits	*Group I, $n = 20$ Long-stay (NIMHANS)*		*Group II, $n = 20$ Day-care (NIMHANS)*		*Group III, $n = 20$ Out-patients (NIMHANS)*		*Comparison and Significance*
	Mean	*s.d.*	*Mean*	*s.d.*	*Mean*	*s.d.*	
Positive symptoms	1.35	1.8100	0.45	0.5104	2.9	2.2219	$x^2 = 24.2583$ df = 2. $P = < 0.001$
Negative symptoms	55	28.3344	45.95	22.2367	59.35	19.7822	$x^2 = 2.54$ df = 2–NS
Mental state deficits	56.25	29.0460	46.35	22.2551	65.6	14.0202	$x^2 = 8.1424$ df = 2. $P = < 0.05$
Cognitive functioning	16.25	7.2756	21.7	5.8499	19.8	6.6495	$x^2 = 5.2$ df = 2.–NS
Current behaviour	8.6	3.9789	5.9	2.8457	8.8	3.75	$x^2 = 10.1786$ df = 2 $P = < 0.05$
Total deficits	78.35	38.7628	60.55	29.3803	84.6	21.6585	$x^2 = 2.8$ df = 2.–NS

TABLE VIII
Comparison of study methods

Method	*Study by Wing & Brown (1970)*	*Study by Johnstone et al (1981)*	*The present study*
Diagnostic criteria	Clinical diagnosis	Feighner's criteria	Research diagnostic criteria
Sample	313 (120+120+73) Females only Age below 60 years Long-stay schizophrenic patients at three hospitals. Comparison was done between 20 patients each.	630 (510+120) Male and female Any age Long-stay and O.P. Schizophrenic patients	96 (20+20+20+20+16) Male and female 20–55 years Long-stay schizophrenic patients at NIMHANS and MH, OP and day-care patients. Long-stay MDP at MH
Exclusion criteria	NIL	NIL	Specific exclusion criteria
Design	Retrospective and prospective	Retrospective and prospective	Retrospective and prospective
Scales for assessment	Clinical rating scale (Wing) Ward Behaviour scale (Wing) Other details	Krawiecka scale Withers & Hinton test for sensorium. Current Behaviour schedule Scheme for brief neurological assessment.	Krawiecka scale SANS MMS WBS Neurological examination proforma (NIMHANS)
Assessment blind?	No	No	No

Results

The sample consisted of 35 males and 61 females. The mean age was 40.68 years (s.d. 9.3, range 26–55). Recorded variables were obtained and deficits assessed in all the patients.

The recorded variables which were used in the calculation of results are shown in Table I. Only one patient in group I and 13 patients in group IV had had insulin coma treatment. The mean number of insulin treatments received by the latter group was 101.1 (range 0-380). Number of insulin treatments poorly correlated with total deficits ($r = 0.2641$).

Table II shows the nature of assessed deficits in each group. All the deficits, apart from positive symptoms, were least evident in patients with manic-depressive psychosis. Among schizophrenic patients, group II had the fewest deficits, group III had the most mental state and total deficits, group IV had the most cognitive and behavioural deficits. Neurological abnormality was observed in only five patients, all with chronic schizophrenia; two of these had tardive dyskinesia, three had Parkinsonian tremor. Neurological deficits were not considered further.

Tables III & IV show the relationships of recorded variables to deficits, and the correlation between the deficits. Recorded variables had poor correlations with deficits.

There was a significant difference in the incidence of negative deficits between groups IV and V (Table V). There was no significant difference between groups I and IV (Table VI). There were significant differences in positive symptoms, mental state deficits and current behaviour between groups I, II and III (Table VII), but the difference in total deficits was not statistically significant. Further analysis shows that the difference in mental state and current behaviour between groups I and III is not significant ($P = >0.5$), whereas the difference in the incidence of positive symptoms remains significant between all three groups ($P = <0.001$).

Discussion

In designing this study, the investigators have leaned on two comprehensive series of investigations, by Wing and colleagues and by Johnstone and colleagues, and its methodology in comparison with theirs is summarised in Table VIII. Our exclusion criteria are unique (compare Wing & Brown, 1970; Johnstone *et al*, 1981; Bhaskaran *et al*, 1972), enhancing the homogeneity of the sample and controlling for those physical variables which may contribute to the development of deficits. Our relatively narrow limits (RDC, age, and specific exclusion criteria) explain our comparatively small sample size.

The present study has a combined prospective and retrospective design. It has the inherent weakness of all retrospective studies with regard to recorded variables. Like any investigation dealing with social factors, it has also an inherent inability to control all the operative variables. However, it has taken care to control most variables relevant to its aims. The investigators were not blind to the diagnoses, or to the psychosocial environments of the patients, but this possible bias was not unique to the present study (Wing *et al*, 1970; Owens *et al*, 1980; Johnstone *et al*, 1981; Johnstone *et al*, 1985).

The results of the study (Table II) indicate that the deficits of chronic schizophrenia extend over a wide range, affecting mental state, cognitive abilities, and current behaviour. We found fewer neurological deficits than other investigators. Johnstone and colleagues reported that 66% of their patients had extrapyramidal symptoms and 9% had other neurological deficits, and that these were related to age and to neuroleptic medication (Owens *et al*, 1980; Johnstone *et al*, 1981). Our very low prevalence of neurological deficits may in part reflect the relatively narrow criteria used to select our patients, none of whom was older than 55 years. However, this aspect of the present study is also compromised by the fact that it did not undertake detailed assessment of 'soft' neurological signs.

Neither neuroleptic medication nor the number of ECTs received by the patient had any significant relationship to deficits (Table III). While a high degree of accuracy about the number of treatments actually received was possible in so far as ECT and insulin coma were concerned, the investigators were less certain about records of past neuroleptic medication. However, our finding that the total amount of medication was not significantly related to deficits does not support the 'alternative hypothesis' of Marsden (1976). Marsden, who challenged the 'disease process' and 'social' hypotheses, put up an alternative viewed from a neurological perspective. He maintained that deficits of schizophrenia such as cerebral atrophy and cognitive impairment were due to drug treatment rather than to incidental or causal pathology. The present study agrees with those of other investigators in suggesting that neuroleptic medication, as such, does not contribute to the development of deficits (Wing *et al*, 1970; Owens *et al*, 1980; Johnstone *et al*, 1981). Taking into consideration the concept of a rapid decline during the first five years and a subsequent plateau in schizophrenic deterioration (Lehman, 1980), the present study analysed the relationship between neuroleptic medication in the first five years and deficits. Our findings indicate that the amount of neuroleptic medication, initial or total, does not have any significant relationship to deficits in chronic schizophrenia. Comparison of deficits in patients treated with neuroleptic drugs and those who have never received them is a much better method than some of investigating the influence of medication.

Our finding that the number of ECTs received by patients does not bear a significant relationship to deficits, and in particular not to cognitive impairment, indicates the transitory nature of the disputed ill-effects of this mode of treatment. Again, comparison of deficits in patients who have received ECT and those who have not is the best way of studying the problem.

Though it has become outmoded, insulin coma treatment has been used in certain of our hospitals. The present study reveals that insulin coma as such is not significantly related to the deficits of chronic schizophrenia, and it has been observed that only prolonged or profound coma has deleterious effects on schizophrenic patients (Kalinowsky *et al*, 1952). Prolonged coma can, of course, be prevented by adequate medical care.

The significant difference in deficits, except with regard to positive symptoms (Table V), between long-stay schizophrenic and long-stay manic-depressive psychotic patients indicates that these deficits, other than positive symptoms, are specific to schizophrenic illness. It also suggests that hospital care as such does not have a significant bearing on the deficits, otherwise the patients with MDP would have developed as many as did schizophrenics.

One must consider the possibility that hospital care is detrimental only to schizophrenic patients, who are specially vulnerable to developing deficits. It is unlikely that care differently given because of specific illness behaviour is responsible. Johnstone and colleagues found that in-patients with affective illness resembled schizophrenic in-patients with regard to cognitive deficits, but differed from them in terms of positive and negative features, and also in most of the behavioural items assessed (Johnstone *et al*, 1985).

The absence of significant differences in deficits between the long-stay schizophrenic patients at NIMHANS and at MH (Table VI) indicates that long-term hospital care and social environment do not have a significant influence on the deficits of chronic schizophrenia. This finding does not agree with that of Wing and colleagues, who found that deficits were significantly different in the schizophrenic patients from three different mental hospitals and were positively related to the degree of social poverty (Wing & Brown, 1970).

Comparison of the three groups of chronic schizophrenic patients at NIMHANS reveals that significant difference between deficits is limited to positive symptoms and to current behaviour (Table VII). Positive symptoms are significantly greater in out-patients, when compared with both long-stay and day-care patients. Similar observations have been made by other authors (Brown *et al*, 1966; Wing, 1978; Johnstone *et al*, 1981; Leff, 1982). Deficits in current behaviour are significantly less in day-care patients, but not significantly different between in-patients and out-patients. The fact that there are significantly fewer deficits, in terms of positive symptoms and current behaviour, in day-care patients may be due either to psychosocial intervention or to other factors, such as the selection criteria for day care.

The conspicuous absence of significant differences in the deficits of chronic schizophrenic patients between the two hospitals, and between the three groups at NIMHANS, might be interpreted as support for a notion that psychosocial methods of treatment have little effect on these deficits. The investigators do not make such a claim on the basis of the present study, which has not attempted to deal with this aspect. To investigate it one would have to manipulate the environment by introducing various forms of psychosocial treatment and subsequently to study the influence of such changes on deficits, in a prospective design. Wing & Brown, who did this, could find definite improvement in only 21% of their patients (Wing *et al*, 1970). Further investigations are needed to find out whether deficits produced by the disease process can be helped by psychosocial modes of treatment.

Granting our methodological difficulties and deficiencies, the results we obtained are evidence to support the following hypotheses: (1) The disease process is responsible for the deficits in chronic schizophrenia. (2) Long-stay hospital care, as such, does not produce these deficits. (3) Physical methods of treatment do not a have significant bearing on them.

The present study is compromised by the following features: the rating was not blind, it was not entirely prospective in design, and all possible operative variables were not controlled. Future research in this area with modified methodology is indicated, although the replication of our findings by studies in which the rating is blind, if theoretically possible, would be impracticable.

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*P. John Mathai MBBS, MD, DPM, *Psychiatrist, Medical College Hospital, Kottayam -8., Kerala, India.*
P. S. Gopinath MBBS, MD, DPM, *Associate Professor, National Institute of Mental Health & Neuro Sciences, Bangalore, India.*

*Correspondence

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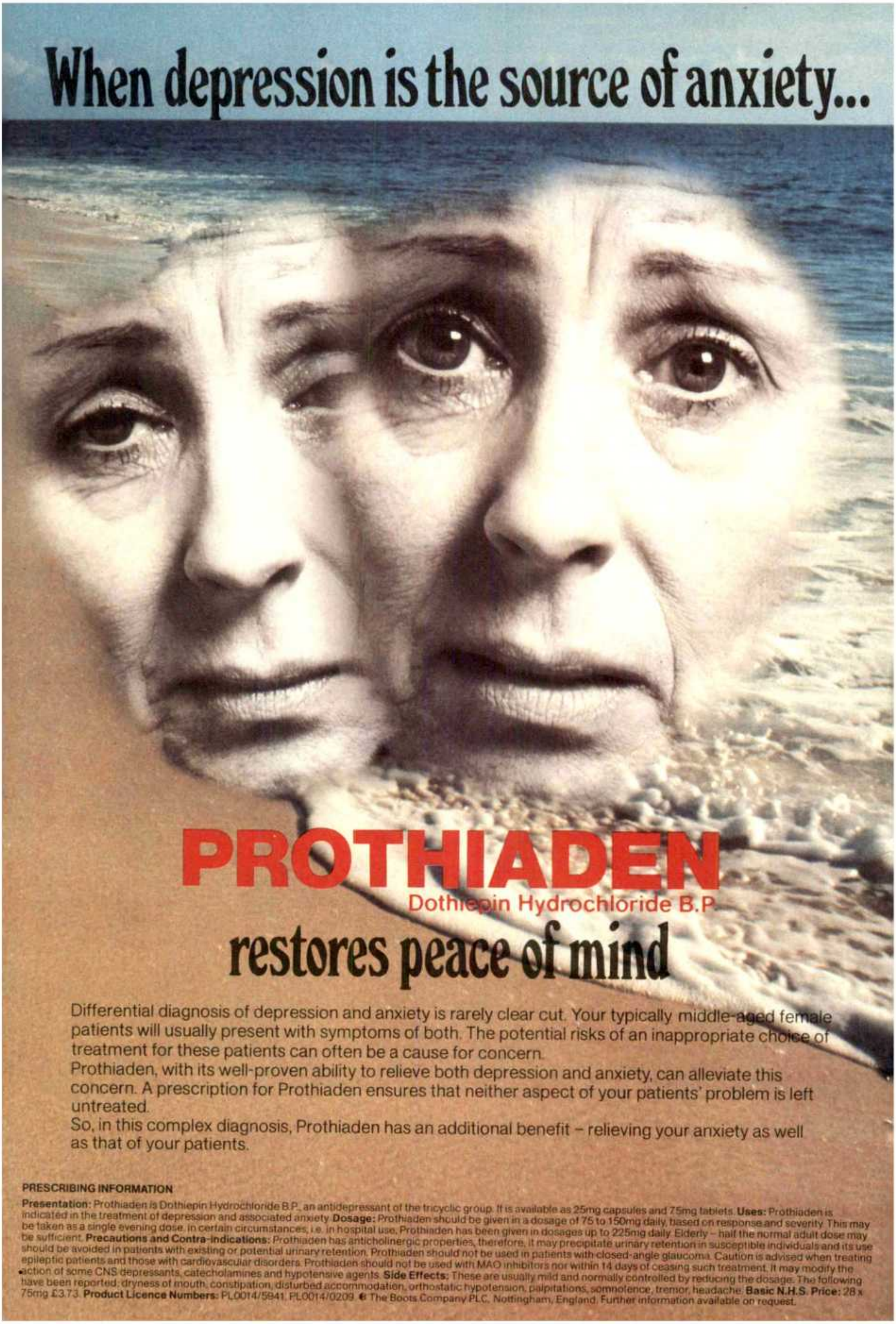

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Clinical Tests of Memory

MICHAEL D. KOPELMAN

This study compared the performance of groups Alzheimer, Korsakoff, and depressed patients and a group of healthy controls at various clinical tests of memory, and wide differences were found in the discriminatory power of the different tests. In addition, the patterns of performance of the Alzheimer and Korsakoff groups differed, and to some extent this was understandable in terms of what is known about the nature of organic amnesia. Depressed patients showed relatively mild impairments, which were not correlated with the severity of their depression.

There have been various attempts to develop memory tests which would differentiate patients with organic disorders from those with functional diagnoses or from healthy controls. The Wechsler Memory Scale (Wechsler, 1945) was developed in part for this purpose, but it is cumbersome to administer and subject to a number of criticisms (Erickson & Scott, 1977; Prigatano, 1978; Schacter & Tulving, 1982; Warrington, 1982). Various other tests or combinations of tests have also been employed for this purpose; in general, evidence of their reliability and concurrent validity (in terms of clinical diagnosis) has been satisfactory (Williams, 1968; Whitehead, 1973; Kendrick *et al*, 1979). In particular, the use of a simple paired-associate learning test has been successfully employed in discriminating dementing from non-dementing elderly patients (Inglis, 1959; Isaacs & Walkey, 1964; Priest *et al*, 1959; Irving *et al*, 1970). More recently, Coughlan & Hollows (1984) demonstrated that a battery of six verbal and visual memory tests could differentiate a mixed group of neurological patients (aged under 65 years) from depressed patients and healthy controls.

There are three principal difficulties with such studies. Firstly, they have usually employed heterogeneous samples of organic patients. There is evidence that the nature of the memory impairment in amnesic patients may differ between diagnostic groups (Lhermitte & Signoret, 1972; Luria, 1976; Cutting, 1978a; Huppert & Piercy, 1979; Butters & Cermak, 1980), and in particular, that the underlying memory deficits may be more extensive in dementing disorders than in the more discrete amnesic syndromes (Miller, 1973; Butters & Cermak, 1980; Weingartner *et al*, 1983; Kopelman, 1985a, b). This means that tests which discriminate for one diagnostic group of patients may not do so for another. Secondly, many studies have also employed a heterogeneous group of functional patients, which gives rise to further problems of interpretation, and these studies have not always used healthy controls as a comparison group to assess the extent of any impairment within the functional sample. Thirdly, most studies have been content to demonstrate statistically significant differences between the mean scores of their groups, and data have not been presented in a form which allows the relative discrimination of different tests to be easily compared (other than in terms of the degree of statistical significance).

A more serious problem is that there is considerably less evidence regarding the validity of everyday tests employed by clinicians than there is regarding more formal, psychometric assessments. Shapiro *et al.* (1956) found that delayed (5-min) recall of a name and address failed to distinguish an elderly group of psychiatric patients with memory impairment from those without amnesic difficulties. Likewise, Warburton (1963) showed that a majority of (mentally) healthy subjects over the age of 40 failed the so-called Babcock sentence test, making its clinical usefulness very doubtful. Withers & Hinton (1971) developed three forms of a Clinical Test of the Sensorium, which included various memory items and which has been employed in a number of clinical studies (Johnstone *et al.*, 1976); their tests did indeed appear to discriminate between patients with a brain syndrome and healthy controls. However, the validation study included only six patients with a brain syndrome, and the mean age of these patients was 20 years older than that of the controls (Hinton & Withers, 1971).

The present study employed a clinical test of memory and orientation and several verbal learning tests to examine discrete groups of dementing, organic amnesic, and functional patients as well as a group of healthy controls. The clinical test of memory and orientation was the Gresham Questionnaire (Institute of Psychiatry, 1973), which was adapted for outpatient as well as inpatient use. The verbal learning tests were selected as being *either (i)* ones commonly employed in clinical practice, *or (ii)* more formal tests, which might easily be administered by a clinician at the bedside. The subject groups were each homogeneous for diagnosis, consisting of Alzheimer patients (dementing group), alcoholic Korsakoff patients (amnesic group), and hospitalised depressed patients (functional group).

Method

Subject groups

Alzheimer patients were diagnosed according to clinical history and examination, with physical investigations to exclude other possible causes of dementia. In addition, it was required that patients should have psychometric evidence of generalised cognitive impairment and CT scan (computerised axial tomographical) evidence of cortical atrophy. None of the patients was hypertensive and none had a history of cerebrovascular disease. Mean duration of symptoms was 2.9 years (range 6 months to 5 years). Mild extrapyramidal symptoms were elicited in 5 out of 16 cases, primitive reflexes in 5 out of 16, and either impaired copying and drawing or frank apraxic signs in 12 out of 13 tested. One further patient was excluded because a changed pattern of symptoms at a 2-year follow-up suggested another cause of dementia. The Alzheimer patients were asked to do Raven's Coloured Progressive Matrices (Raven *et al*, 1977), and Intelligence Quotients (IQ) were obtained from Raven's age-related tables. If the patient's IQ was ≥75 on this screening, he or she was retested on those sub-tests of the Wechsler Adult Intelligence Scale (WAIS) employed by Savage *et al* (1973) and a pro-rated full scale IQ obtained. The patient with the highest IQ (full scale = 116) had deteriorated by 21 points over an 11-month period. As reported elsewhere (Kopelman, 1985b), Alzheimer patients had a significantly larger mean ventricular-brain ratio (VBR) on CT scan ($t = 4.36$, $P < 0.001$) and a significantly greater rating of cortical atrophy ($t = 3.61$, $P < 0.01$) than the Korsakoff patients.

Korsakoff patients were selected to conform as closely as possible to the acute onset group described by Cutting (1978b). Eight out of 9 cases in which the mode of onset was known had had an acute onset of the disorder (i.e. less than 8 weeks between onset of symptoms and admission). The patients had a similar age- and sex-distribution to Cutting's sub-group, reflecting the different age- and sex-distribution of this disorder from Alzheimer-type dementia. With respect to Wernicke symptoms, 12 out of 16 cases had a recorded history of nystagmus and/or ophthalmoplegia, all cases had a history of ataxia and of disorientation in time, and 10 a history of peripheral neuropathy. All had an alcoholic aetiology, with a mean duration of heavy alcohol abuse of 24 (range 10 to 37.5) years. Median time 'dry' was 24 weeks (range 8 weeks to 12 years), and although some patients had shown a degree of improvement on repeated psychometric testing, all were severely incapacitated by their memory disorder—either living in institutions or heavily dependent on institutional support.

Depressed patients all had a clinical diagnosis of a primary depressive disorder: mood change was prominent and biological symptoms invariably present. Onset had been acute or subacute in all cases, and the severity of the depression was such that they were all hospitalised in-patients during a 3-month period (August to October 1984). Mean Hamilton Depression score (Hamilton, 1960) was 28.1 ± 4.1 (range 20–35). The sample was selected so that it would overlap in terms of sex-distribution (8 M:8 F) and age (mean 60.6, range 42 to 74 years) with the Alzheimer and Korsakoff patients. Patients who had had ECT within the last 3 years, any evidence of organic impairment, or any history of recent alcohol abuse were excluded from the sample. Thirteen of the 16 patients were taking antidepressant medication, one lithium, six phenothiazines, and seven benzodiazepines (usually as night sedation); only two patients were yet to be started on any medication. In none of the patients were memory symptoms so prominent that a diagnosis of pseudodementia had been considered; however, on direct questioning, virtually all the patients complained of forgetfulness.

Control subjects were selected to match the depressed patients and to overlap with the Alzheimer and Korsakoff patients in terms of sex- (8 M:8 F) and age-distribution (mean 60.4, range 38 to 73 years). It was possible to subdivide the control group into an Alzheimer comparison group (2 M:6 F, mean age 66.25, range 55 to 73 years) and a Korsakoff comparison group (6 M:2 F, mean age 54.5, range 38 to 67 years), although this did not prove necessary for present purposes. The control subjects consisted of healthy elderly subjects living in sheltered accommodation and younger subjects from the MRC Applied Psychology Unit Research Panel and from the Institute of Psychiatry non-academic staff.

Tests employed

Gresham questionnaire (Shapiro *et al*, 1956; Institute of Psychiatry, 1973): a clinical interview designed to assess memory and orientation (especially in the elderly), and, in the present study, adapted for outpatient as well as inpatient use. The amended questionnaire is available from the author on request. Maximum score = 43.

Wechsler logical memory (Wechsler, 1945): recall of the contents of a short paragraph, immediately and after 45 min delay. Maximum score = 23. Percentage retention = 45 min score ÷ immediate score.

Paired-associate learning (Isaacs & Walkey, 1964; Priest *et al*, 1969): a very simple paired-associate test, previously found useful in assessing elderly and dementing patients, and consisting of three very easy paired-associates (e.g. east–west) and three more difficult paired associates (e.g. gold-lead). Maximum score = 18.

Name and address (Withers & Hinton, 1971): an 8-word name and address to be recalled immediately (repeated by the examiner until one perfect recall or a maximum of five learning trials had occurred) and after 4 min delay. Maximum score = 8.

Anomalous sentences test (adapted from Newcombe & Marshall, 1967; Newcombe, 1969): Subjects were asked to repeat immediately back to the examiner two normal sentences and six anomalous sentences. Four sentences had normal syntax but aberrant semantics (e.g. 'Colourless green ideas sleep furiously'); one sentence provided the opportunity for semantic confusions ('Wasn't the rich uncle advised by the nice manager?'); and one was a random word-string ('Not in tree to the ran lake with'). All eight sentences were read to the subject before testing proper began. Each sentence was then re-read to the subject, who was required to repeat it verbatim, and there was a maximum of four learning trials for each sentence. Maximum score for test (perfect recall) = 32.

Digit span forward (Wechsler, 1945): assessed according to the procedure of the Wechsler memory scale. Performed on two occasions (usually a week apart) and mean score taken.

Supraspan (Zangwill, 1943; Miller, 1973): digit span was established, and then the subject was required to learn a sequence two digits greater than his/her immediate span. Number of learning trials for perfect recall recorded up to a maximum of 10.

Babcock sentence (Babcock, 1930; Zangwill, 1943): number of learning trials required for perfect recall of the Babcock sentence, up to a maximum of 10.

Results

Table I shows that the four groups were approximately matched for premorbid IQ, as evaluated by a reading test (Nelson & O'Connell, 1978). Whilst the Alzheimer group had a substantially lower current IQ ($F = 24.3$, $P < 0.001$), the other three groups did not differ significantly from one another ($F = 0.94$, NS). The Korsakoff patients and the depressed group both showed, at most, very trivial deterioration in terms of general intellectual function.

Table II shows the mean scores of the four groups at all the tests except Supraspan and the Babcock sentence. All

TABLE I
Summary description of samples

	Healthy controls (C) (n = 16)	*Depressed patients (D) (n = 16)*	*Korsakoff patients (K) (n = 16)*	*Alzheimer patients (A) (n = 16)*
Sex ratio	8 M:8 F	8 M:8 F	13 M:3 F	4 M:12 F
Mean age (years)	60.4(±10.5)	60.6(±9.2)	56.5(±7.1)	65.6(±6.8)
(range)	(38–73)	(42–74)	(38–66)	(56–75)
Premorbid IQ estimate by NART[1,2] mean (±s.d.)	108.5(±9.3)	107.6(±8.3)	106.3(±11.5)	105.9(±9.6)
Full scale IQ[3] mean (±s.d.)	107.3(±12.3)	103.7(±5.9)	101.8(±12.3)	71.4(±17.2)
(range)	(84–124)	(87–122)	(81–124)	(48–116)
Deterioration index[2] (NART − IQ) Mean (±s.d.)	0.3(±6.9)	3.9(±7.5)	5.4(±8.7)	32.7(±18.4)

[1] New Adult Reading Test: Nelson & O'Connell (1978).
[2] Data available for $n = 14$ for each of controls, Korsakoffs and Alzheimers: $n = 16$ for depressed patients.
[3] For method of determination in the Alzheimer group, see text.

TABLE II

Mean scores of clinical groups on memory tests, and statistical significance of differences between groups

	Healthy controls (C)	*Depressives (D)*	*Korsakoffs (K)*	*Alzheimers (A)*	*ANOVA*		*Non-organic*^{1} *versus organic*^{2}*	*C versus D**	*D versus K**	*K versus A**
					F	*P*				
Gresham										
Orientation	8.0	7.7	3.4	5.0	33.2	<0.001	<0.001	NS†	<0.001	<0.05
Remote personal	11.7	10.9	6.0	6.9	63.75	<0.001	<0.001	<0.02†	<0.001	NS
Recent personal	10.1	10.0	2.1	3.4	139.5	<0.001	<0.001	NS	<0.001	<0.05
General events	10.6	9.4	3.9	3.8	54.5	<0.001	<0.001	NS	<0.001	NS
Total score	40.0	38.0	15.3	19.2	170.2	<0.001	<0.001	0.02†	<0.001	<0.05
Logical memory										
Immediate recall	12.1	9.3	4.1	3.2	46.5	<0.001	<0.001	<0.02	<0.001	NS
Delayed recall	9.9	6.8	0.4	0.3	84.3	<0.001	<0.001	<0.01	<0.001	NS
Percentage retention	81.8	73.1	9.8	9.4	149.8	<0.001	<0.001	NS	<0.001	NS
Paired-associate learning										
Very easy pairs	8.9	8.3	8.1	5.6	20.6	<0.001	<0.001	<0.05†	NS	<0.001
More difficult pairs	8.3	6.9	5.1	3.25	15.0	<0.001	<0.001	<0.02†	<0.05	NS
Total score	17.2	15.2	13.1	8.8	22.5	<0.001	<0.001	<0.02†	NS	<0.01
Name and address										
Delayed recall (4 min)	6.9	6.0	2.1	1.7	33.1	<0.001	<0.001	NS	<0.001	NS
Anomalous sentences										
Total Score	26.1	25.8	23.9	15.8	11.8	<0.001	<0.001	NS	NS	<0.001
Digit span										
Forward	6.4	6.7	6.5	5.4	**6.5	<0.001	<0.02	NS	NS	<0.01

*t-tests. Two-tailed level of significance given for all tests cited.

**Co-varying for age = 5.65; $P < 0.005$.

†Mann Whitney U-test employed when variance within groups could not be assumed to be homogeneous (tested by F_{max} statistic).

[1] C+D.

[2] K+A.

TABLE III

Number of subjects in each group failing to score at cut-off point on memory tests (n = 16 in each group)

	Healthy controls (C)	*Depressives (D)*	*Korsakoffs (K)*	*Alzheimers (A)*	χ^2	*P*	*Non-organic*[1] *versus organic*[2]	*C versus D**	*D versus K**	*K versus A**
Gresham										
Orientation < 7	0	1	15	12	44.2	<0.001	<0.001	NS	<0.001	NS
Remote personal < 10	0	1	16	15	56.5	<0.001	<0.001	NS	<0.001	NS
Recent personal < 8	0	0	16	16	64.0	<0.001	<0.001	NS	<0.001	NS
General events < 7	0	0	15	13	50.3	<0.001	<0.001	NS	<0.001	NS
Total score < 32	0	0	16	16	64.0	<0.001	<0.001	NS	<0.001	NS
Logical memory										
Immediate < 7	0	5	15	15	42.6	<0.001	<0.001	NS	<0.001	NS
Delayed < 5	0	3	16	16	54.2	<0.001	<0.001	NS	<0.001	NS
Retention < 50%	0	0	16	16	64.0	<0.001	<0.001	NS	<0.001	NS
Paired-associates										
More difficult pairs < 6	0	3	8	12	23.0	<0.001	<0.001	NS	NS	NS
Total score < 14	0	3	8	14	30.3	<0.001	<0.001	NS	NS	NS
Total score < 16	3	8	10	15	18.8	<0.001	<0.001	NS	NS	NS
Name and address										
Learning trials > 2	2	3	2	13	25.0	<0.001	<0.01	NS	NS	<0.001
Delayed recall score < 6	0	7	15	14	37.1	<0.001	<0.001	<0.02	<0.01	NS
Anomalous sentences										
Score < 16	1	0	1	8	19.4	<0.001	<0.01	NS	NS	<0.02
Score < 22	4	3	5	13	16.5	<0.001	<0.01	NS	NS	<0.02
Supraspan (+2)										
Learning trials > 5	11	12	14	14	2.6	NS	NS	NS	NS	NS
Learning trials > 10	5	11	8	13	9.4	<0.05	NS	NS	NS	NS
Babcock sentence										
Learning trials > 5	9	14	13	16	10.7	<0.02	NS	NS	NS	NS
Learning trials > 10	6	8	12	15	13.2	<0.01	<0.001	NS	NS	NS

[1] C + D.
[2] K + A.
*χ^2 with Yates's correction.

the tests discriminated at a very high level of statistical significance between the non-organic (control+depressed) and organic (Korsakoff+Alzheimer) groups. The most discriminating tests were the Gresham in terms of recent personal memory ($F=139.5$) and total score ($F=170.2$) and Wechsler logical memory in terms of percentage retention ($F=159.8$). Despite this, some interesting and important differences between the tests emerged when the performance of individual groups was compared (see Table II).

Depressives scored lower than healthy controls at all tests except digit span. Differences were small, but were statistically significant for Gresham remote personal memory and total score, Wechsler logical memory (immediate and delayed recall), and paired-associate learning. There were no significant correlations between the depressives' Hamilton scores and their performance at any of the memory tests.

Both Korsakoff and Alzheimer patients were significantly impaired, relative to depressives, at the Gresham and logical memory tests, paired-associate learning of more difficult pairs, and delayed recall of a name and address. However, there were no significant differences between the Korsakoff and depressive groups at digit span, paired-associate learning of very easy pairs, or the anomalous sentences test.

The Alzheimer group was significantly impaired on each of these last three tests, relative to the Korsakoff group, and also relative to the other two groups. The only tests at which Alzheimer patients scored significantly higher than Korsakoff patients were the orientation and recent personal memory scales of the Gresham, and the Gresham total score.

Table III shows the relative discrimination between the groups by the different tests at selected cut-off points. Data for the Supraspan and Babcock sentence tests are included, showing the numbers of subjects in each group who failed at these tests after five and after 10 learning trials. The cut-off points for the other tests are those which gave the best discrimination between the non-organic and the organic groups. Also shown for the paired-associate total score is the cut-off point (less than 16) which Priest *et al* (1969) reported to discriminate maximally between organic and functional patients.

The three most discriminating tests (Gresham recent personal memory score below 8, Gresham total score below 32, and Wechsler logical memory percentage retention less than 50%) all gave perfect differentiation between the non-organic and organic groups in the present sample. Most of the other tests gave statistically significant discrimination between the non-organic and organic groups, but the paired-associate learning test was unsatisfactory, in that it failed to discriminate significantly between depressed and Korsakoff patients. The Supraspan and Babcock sentence tests gave very poor discrimination.

Using these cut-off points, more depressives scored within the impaired range on most tests than did healthy controls, but the difference was statistically significant only for delayed recall of a name and address. Alzheimer patients were impaired significantly more frequently than Korsakoff patients (and also than the other two groups) at learning a name and address within two trials and at the anomalous sentences test.

Discussion

The samples employed in the present study were relatively small, but, unlike those in many other studies, homogeneous for diagnosis. Moreover, the Alzheimer and Korsakoff groups both displayed a severe memory impairment (revealed by their clinical histories, as well as by their Gresham and logical memory performance). Those tests which failed to differentiate these patients clearly from depressives or healthy controls are therefore very unlikely to be of diagnostic value in assessing individual cases with a milder degree of memory impairment.

Non-organic versus organic groups

Although virtually all the tests differentiated between these two groups at a statistically significant level, the results revealed wide variability in their discriminatory power.

The Gresham and Wechsler logical memory tests gave by far the best discrimination. Both tests have previously been validated in studies employing a prospective component (Shapiro *et al*, 1956; Whitehead, 1973). This indicates the clinical usefulness of a memory and orientation questionnaire such as the Gresham, but also reminds us that impairment on such a scale is by no means diagnostic of dementia: the Korsakoff group scored significantly lower in terms of total score than the Alzheimer group ($t=2.16$, $P<0.05$). The usefulness of the Wechsler logical memory test is corroborated by the recent finding of Sunderland *et al* (1983) that impairment at this test is correlated more strongly with the severity of everyday memory symptoms reported by questionnaire than is performance at other psychometric tests. Sunderland *et al* (1983) examined severe head injury patients, and the memory questionnaire was completed in each case by both the patient and a relative.

Delayed recall of a name and address also gave satisfactory discrimination; and the paired-associate learning test differentiated between the non-organic and organic groups, as Priest *et al* (1969) had earlier found. However, this latter test illustrated the hazards of comparing heterogeneous groups, because the total test score failed to differentiate at a statistically significant level between the depressed and Korsakoff samples. This particular paired-associate test contains word-pairs of a very high or a somewhat lower degree of association. Recall of paired-words of very high associative status (eg east-west) can hardly be construed as a test of new learning, and indeed it has previously been reported that Korsakoff patients are relatively unimpaired at recalling high-associate paired words (Wechsler, 1917; Warrington & Weiskrantz, 1982). The present results were consistent with that observation: the Korsakoff patients were unimpaired at recalling the very easy pairs (of high associative status), but were significantly impaired at the more difficult pairs (of lower associative status). By contrast, Alzheimer patients were impaired at recalling both the very easy and the more difficult paired associates.

The Supraspan and Babcock sentence tests gave very poor discrimination, the results confirming Warburton's (1963) observation that healthy controls over 40 frequently perform very poorly at such tests. Though these tests are still widely employed in clinical practice, the present results suggest that they should be abandoned.

Controls versus depressives

Various previous authors have noted impairment by depressed patients relative to healthy controls on memory and other cognitive tests (Whitehead, 1973; Weingartner *et al,* 1981). Cohen *et al* (1982) reported that the degree of impairment was closely related to the severity of depression, as assessed by various rating scales (including the Hamilton), whereas Friedman (1964) and Coughlan & Hollows (1984) found that impairment was mild and had no significant association with the severity of depression. The present study is consistent with the latter observations. Depressives performed worse than healthy controls at all tests except digit span, the differences being statistically significant in some instances, but the degree of impairment tended to be relatively small and there was no significant correlation with Hamilton scores.

Alzheimer versus Korsakoff patients

The tests at which Alzheimer, but not Korsakoff patients were severely impaired were those which required immediate recall of a relatively small quantity of verbal material: viz, digit span, immediate recall of a name and address, recall of very easy paired-associates, and the anomalous sentences test. It has been argued elsewhere that Alzheimer, but not Korsakoff patients have a severe impairment of immediate or primary memory, also known as short-term or working memory (Miller, 1971, 1973; Wilson *et al,* 1983; Kopelman, 1985a, b). The primary memory store is assumed to have a very limited capacity, and to hold information for a few seconds only before most of it is filtered out and decays, a relatively small proportion being encoded into a secondary, more permanent memory store (Hunter, 1964; Craik, 1971; Baddeley, 1976). Given that the present Alzheimer patients were not dysphasic, an impairment of primary (or working) memory may best account for their deficit at those tests which Korsakoff patients were able to perform satisfactorily. This interpretation with respect to the anomalous sentences test will be discussed in greater detail elsewhere (Kopelman, 1986).

Weingartner *et al* (1983) have recently proposed that the memory disorder of Alzheimer-type dementia differs from that of Korsakoff's syndrome in that it involves a deficit of semantic as well as of episodic memory. Semantic memory refers essentially to stored, conceptual knowledge of the world, as distinct from a stored record of personal experiences (Tulving, 1972; Baddeley, 1964). As such, it is a conglomerate term, encompassing, for example knowledge of the use of language and syntax, and of personal details (e.g. date of birth, height, and weight), and worldly information (e.g. being able to name the present prime minister). The present results on relevant Gresham questionnaire items indicate that the Korsakoff group's conceptual knowledge of the world was, in some respects, at least as impaired as that of the Alzheimer group. Thus, a crude distinction between the memory disorders of the two conditions, based on the episodic/semantic dichotomy, is unlikely to be very useful.

Conclusion

The present study revealed very wide differences in the discriminatory power of various clinical tests of memory: the most satisfactory were of memory and orientation questionnaire (the Gresham) and the Weschler logical memory test. Other tests—Supraspan and the Babcock sentence—were very unsatisfactory and would best be abandoned.

To a substantial degree, the differing patterns of performance by the Alzheimer and Korsakoff groups could be understood in terms of what is already known about the nature of organic amnesia. Alzheimer, but not Korsakoff, patients were impaired at tests which appeared to depend heavily upon an intact immediate or primary memory. Moreover, Korsakoff patients were able to recall paired-associates without difficulty when the pairs were of high associative status. This study confirmed those previous ones which have suggested that, although depressed patients are impaired at memory tests, the impairment is not marked and is not correlated with the severity of the depression.

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Michael D. Kopelman, BA, MB, MRCPsych, ABPS. *Wellcome Trust Lecturer, Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF.*

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Respiratory Control in the Treatment of Panic Attacks:
Replication and Extension with Concurrent Measurement of Behaviour and pCO_2

PAUL M. SALKOVSKIS, DAVID R. O. JONES and DAVID M. CLARK

A case series is reported in which nine patients who experienced phobic and/or non-phobic panic attacks were given a cognitive-behavioural treatment based on the supposition that catastrophic interpretations of sensations produced by hyperventilation played an important role in their attacks. Large and rapid reductions in panic attack frequency and questionnaire report of fear were observed. Patients' resting pCO_2 was significantly lower than controls and rose to normal levels during treatment.

Panic attacks, defined as relatively rapid increase in anxiety or fear accompanied by a wide range of somatic symptoms, have previously been described surprisingly infrequently in the psychiatric literature. Most often, they have been discussed in association with anxiety states and agoraphobia. The advent of DSM III and the heavy emphasis this places on panic attacks in the classification of anxiety disorders, has led to an increased interest in the nature and treatment of panic attacks in general and the newly created category of 'Panic Disorder' in particular. Several writers (Kerr *et al*, 1937, Lum 1976, Gibson 1978, Clark 1979, Hibbert 1984) have pointed out that the physical sensations associated with a panic attack are very similar to those produced by hyperventilation, and have further suggested that hyperventilation may play an important role in the production of panic attacks. Clark *et al* (1985) utilised a model in which it was suggested that some individuals increase their respiratory ventilation when under stress. This increase in ventilation 'blows off' carbon dioxide from the lungs, leading to a decrease in the partial pressure of CO_2 in the blood and an increase in pH of the blood. These changes produce a wide range of unpleasant bodily sensations which are responded to with apprehension, either because they are perceived as frightening in themselves or because they augment the fear already elicited by other stimuli. The increased apprehension then elicits further increases in ventilation and so on round in a vicious circle, which culminates in a panic attack.

Consistent with the above model it has been found that (1) some individuals overbreathe when anxious (Seuss *et al*, 1980, Salkovskis *et al*, 1986); (2) individuals who score high on Eysenck's neuroticism scale, and so are said to be vulnerable to developing panic attacks, are more distressed by a brief period of hyperventilation than individuals who score low on neuroticism (Clark & Hemsley 1982); (3) treatments aimed at controlling hyperventilation appear to reduce the frequency of 'anxiety attacks' in medical patients referred to a chest clinic (Lum 1976) and the frequency of panic attacks in psychiatric out-patients (Clark, *et al.* 1985). The treatment used by Clark *et al*, (1985) consisted of reattribution of panic attacks to hyperventilation and training in respiratory control procedures. It produced a substantial and rapid reduction in panic attack frequency, as measured by a daily diary. This improvement took place despite evidence that avoidance behaviour had not changed, and thus provided strong support for the hypothesis that this improvement was not a result of increased exposure levels. Furthermore, self-ratings of anxiety during a behavioural test showed a considerable and significant reduction, which could not be attributed to repeated testing. Outcome data included a two-year follow-up, with improvement having been maintained. It is important to note that results indicated that patients who experienced panic attacks but who did not show any consistent patterns of avoidance did extremely well on this treatment, and had ceased to experience panic attacks at the end of the study. This constitutes a group for whom at present there is no effective behavioural treatment. One of a number of important questions raised relates to whether patients with panic attacks had a lowered resting pCO_2 compared to normals, in the way described by Lum (1976), and, if so, whether treatment actually resulted in an increase in resting levels. The present study was therefore a replication and extension of this first study, with the inclusion of repeated measures of pCO_2 taken at baseline and during treatment, together with appropriate methodological checks on this measure itself.

Method

Subjects These were nine (8F:1M) consecutive referrals from general practitioners and consultant psychiatrists to a Health Service psychology department who met the following criteria: (1) they suffered from panic attacks, and these were considered to be their main problem; (2) during attacks, they experienced at least 3 bodily symptoms characteristic of hyperventilation, from a list including breathlessness, dizziness, faintness, numbness, parasthesiae, tremor, tight muscles, tachycardia, nausea, dry mouth, sweating, weakness, and hot flushes (Clark & Hemsley 1982); (3) there was no evidence of a life-threatening or metabolic illness, or previous diagnosis of a psychotic condition. Mean age was 30.4 years, (s.d. 5.7, range 26–44), and they had been suffering from panic attacks for a mean of 6.6 years (s.d. 5.3 years, range 1.5–18 years). As in the previous study, patients were divided into two groups. Situationals ($n = 5$) were patients who reported that there were certain situations in which they consistently experienced anxiety. Many, but not all of their panic attacks occurred in these phobic situations, which fell mainly into the agoraphobic and social phobic clusters in the Marks & Mathews questionnaire. Non-situationals ($n = 4$) were unable to identify any situations which were consistently associated with anxiety. Seven patients were taking psychotropic medication at the time of referral; (three benzodiazepines, three tricyclics and benzoidiazepines, one both a benzodiazepine and a beta blocker). Drug intake had been constant for some weeks before start of baseline in all cases.

Outcome measures (1) Panic attack diary. Patients kept a record of their overall anxiety for each day, as well as the number and severity of panic attacks they experienced. Overall anxiety for the day was rated on a 100-point visual analogue scale, anchored at either end with the words "I was not at all anxious" and "I had the most anxious day I have ever had." The wording used on the diary for panic attacks was:

"Record here any *attacks* of anxiety you experience during the day. In an attack, anxiety builds up fairly quickly. Gradual build-ups of tension are not considered attacks. In the severity column, give a rating for how anxious you were during *each* attack, and in the frequency column write the number of attacks you have in the day."

The scale used was a 100-point visual analogue scale, anchored at either end by the words "I was not at all anxious" and "I was the most anxious I have ever been". Patients were instructed to fill out the severity rating as soon as possible after each attack, and the overall daily anxiety and frequency of panic attacks just before going to bed each night. As already stated, patients were only included in the study if they experienced at least three bodily symptoms characteristic of hyperventilation during their attacks.

(2) Marks & Mathews (1979) Fear questionnaire: This questionnaire contains three scales (Avoidance, Anxiety/Depression, Global Distress) and has been shown (Marks and Mathews 1979) to be a sensitive measure of clinical improvement.

(3) Beck Depression Inventory: This questionnaire has been shown to be a sensitive measure of clinical depression (Beck & Beamsderfer, 1974) and was included to allow assessment of the severity of patients' depressive symptoms.

Procedure An interrupted time series design was used, with repeated measures of clinical state taken on a daily and session by session basis. Additionally, measures of mixed venous pCO_2 were taken on each attendance at the clinic. Patients were sent a diary for the recording of panic attacks along with their first appointment letter, and asked to continue this throughout treatment. At the first interview, patients were screened for the inclusion criteria, a full clinical assessment was carried out, and the Beck Depression Inventory (Beck & Beamsderfer 1974) and Marks & Mathews Fear Questionnaire (Marks & Mathews 1979) were administered. *All patients were given strict instructions not to change their current lifestyle by any increase in their exposure to feared situations during the period of pure respiratory control treatment.*

After a further assessment, and at least 4 weeks after starting to fill in panic diaries, they were seen for the first treatment session. This involved (i) instructions in the use of a paper bag for rebreathing, (ii) two minutes of forced ventilation in a relatively standardised fashion ('provocation test'), (iii) brief rebreathing with the bag, (iv) completion of a Similarities Questionnaire (Clark *et al.* 1985) which assessed the similarity between the effects of overbreathing and naturally occuring panic attacks and (v) completion of a Symptoms Rating Sheet (Clark & Hemsley 1982) which covers most of the well known effects of hyperventilation. These procedures provided a basis for the discussion and re-attribution of somatic symptoms associated with panic attacks to stress-induced hyperventilation, rather than the more catastrophic things which are usually feared, (such as heart disease, epilepsy, fear of going mad, or fear of making a fool of oneself). Training in paced breathing was commenced with the aid of a tape set at 12 breaths per minute. Following satisfactory performance with this training, the patient was provided with copies of the tape and a handout reiterating the relationship between respiration and anxiety, and reviewing the instructions regarding the application of paced breathing in the control of anxiety. All patients were directed to practise with the tape daily, and attempt to apply the training to control panics if they noticed themselve starting to become panicky. They were also reminded at this point of the importance of not increasing their exposure to feared situations above pre-treatment levels. A second treatment session, within the next five days, continued and extended the breathing training, and further homework instructions were provided. Two more brief sessions, at weekly intervals, continued the respiratory training and homework instructions. (A more detailed description of the treatment procedures can be found in Clark *et al* (1985).)

One week later, (4 weeks after the first training session), all assessments were repeated, and at this point, graded exposure instructions were added to respiratory control if considered appropriate for the situational group. Further assessments were carried out at three months and six months. There was a total of 9 sessions in which some treatment took place; four during pure respiratory treatment (1 hr–30 mins each) and five during exposure/follow up (45 mins–15 mins).

Measurement of pCO_2 The technique used for the measurement of pCO_2 was a shortened version of Cambell & Howells (1962) rebreathing technique. This has been shown (Clark, 1979) to have a high test-retest reliability ($r = 0.95$), which compares favourably with the test-retest reliability of the full technique ($r = 0.97$). It should be noted that pCO_2 is the most accurate measure of ventilation. Clinicians without access to pCO_2 measurement can gain a rough indication of overbreathing by observing respiratory rate. However, it should be noted that some patients substantially reduce respiratory depth while increasing rate, and hence overall do not hyperventilate. Validation of the short version against the full technique gives a highly satisfactory figure of $r = 0.89$. The shortened version uses a 2-litre bag and valve arrangement, the bag being half-filled with a mixture of 95% O_2 and 4% CO_2. Subjects are asked to empty and fill the bag six times within 30 seconds, the last exhalation being collected and analysed. This is a measure of arterial pCO_2 once a constant correction is applied. Resting arterial pCO_2 was measured on each occasion that patients attended the clinic.

At the first assessment interview, two measures were taken. In a second pre-treatment session, five pCO_2 measures were taken, with ten minutes between each measurement. This served both to check reliability *per se* and also to investigate whether becoming familiar with the technique itself results in increased pCO_2 readings as an artefact of reduced anxiety about the measurement procedure itself. Clearly, such an effect, if it were present, would complicate the interpretation of any changes in pCO_2 as treatment progressed. During the first treatment session, recordings were taken twice at rest to give a measure of longer-term stability, when compared with the immediately preceding session. A further reading was taken immediately after the end of the provocation test to evaluate change from baseline, then ten minutes later to give a recovery measure. During treatment, measures were taken at the start of each session; pCO_2 measures were taken using an ADC type SS1 infrared gas analyser, which was calibrated on each occasion before use.

Results

Statistical analysis The results were analysed using a repeated measures analysis of variance (BMDP P2V) (Dixon *et al*, 1983), with the division between situation-specific and non-situation specific as the grouping variable. Due to the strong likelihood of serial dependency in repeated measures, significance was evaluated using the Greenhouse-Geisser correction of degrees of freedom whenever a significant value was obtained on the sphericity test (Keselman & Rogan 1980). The epsilon factor used to obtain this conservative estimate was subsequently applied in the calculation of Newman-Keuls tests.

Effect of treatment on ratings and diaries Because the study is a replication of Clark *et al* (1985), the data for panic attack frequency together with the questionnaire results are of particular interest, as these were the main outcome measures used in this previous study.

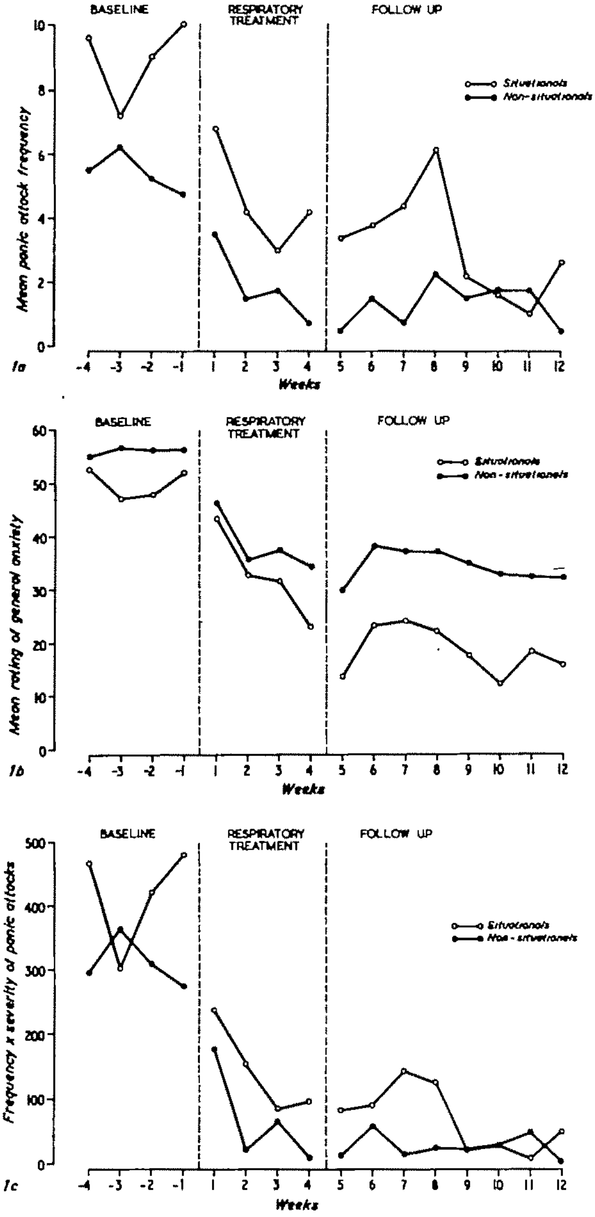
Figs 1a and 1b show the effect of treatment on diary measures of panic attack frequency and daily rating of general anxiety (the latter not having been examined in the first study). There were no significant group x treatment interaction effects for clinical outcome or pCO_2 measures.

The first comparison examined the effect of the four weeks of respiratory control, as compared to the four weeks of baseline. For panic attack frequency, there was a significant main effect of time ($P < 0.01$). Newman-Keuls tests indicated that there were no significant differences among the four baseline points, and that the frequency of panic attacks during all weeks of the treatment was significantly reduced, when compared to all weeks of baseline ($P < 0.05$ in each case). Treatment effects were maintained during the graded exposure period.

The same form of analysis was used for general anxiety ratings, with the comparison of baseline to respiratory treatment alone yielding a significant effect of time, $P < 0.05$. Newman–Keuls tests indicated that by the fourth week of respiratory control, general anxiety was significantly less than all baseline weeks ($P < 0.05$). Results indicated that treatment effects were maintained during the subsequent graded exposure.

Besides keeping a record of the number of panic attacks experienced, patients also rated the severity of each attack. Inspection of severity ratings indicated that respiratory control was associated with a decrease in the severity of panic attacks, as well as with a decrease in frequency. Mean panic attack severity was 51 during the baseline period, dropping to 42 during the period of pure respiratory control ($t_4 = 4.62$, $P < 0.01$). As respiratory control reduces the severity of panic attacks it could be argued that Figure 1a, which simply plots frequency of attacks, underestimates the effectiveness of the treatment. A fairer estimate is perhaps provided by Figure 1c, which plots frequency X severity. Table I illustrates treatment outcome as measured by questionnaire during baseline, at the end of four weeks of the respiratory based treatment, eight weeks later (during which time exposure instructions had been given to the situational group), and then six months later.

Analyses of variance were used to compare pre-treatment values with those obtained at the end of the period of respiratory training. Significant effects of time were detected for the Marks & Mathews (M&M) total avoidance score ($P < 0.05$) M&M, depression/anxiety scale



FIGS. 1a, 1b and 1c. Weekly panic attacks and generalised anxiety ratings in situational ($n=5$) and non-situational ($n=4$) patients.

($P=0.001$), M&M global rating of distress ($P<0.05$), and the Beck Depression Inventory ($P<0.05$). All questionnaire measures therefore indicated a significant improvement as compared to baseline following four weeks of respiratory training alone. Analysis of the follow-up results of the questionnaires indicated that treatment effects were maintained and improved upon for these measures.

Measures of pCO_2 within and between sessions The correlations between the five pCO_2 measures obtained during the second assessment session confirm the stability of the

TABLE I
Mean scores on questionnaires in each treatment phase

Scale	Baseline	Week 4	Week 12	6 Month FU
M&M avoidance	53.2	34.4	28.44	25.11
M&M anx/dep	20.0	13.2	9.22	7.56
M&M global distress	4.7	3.11	2.11	1.56
BDI	16.33	9.78	6.56	5.89

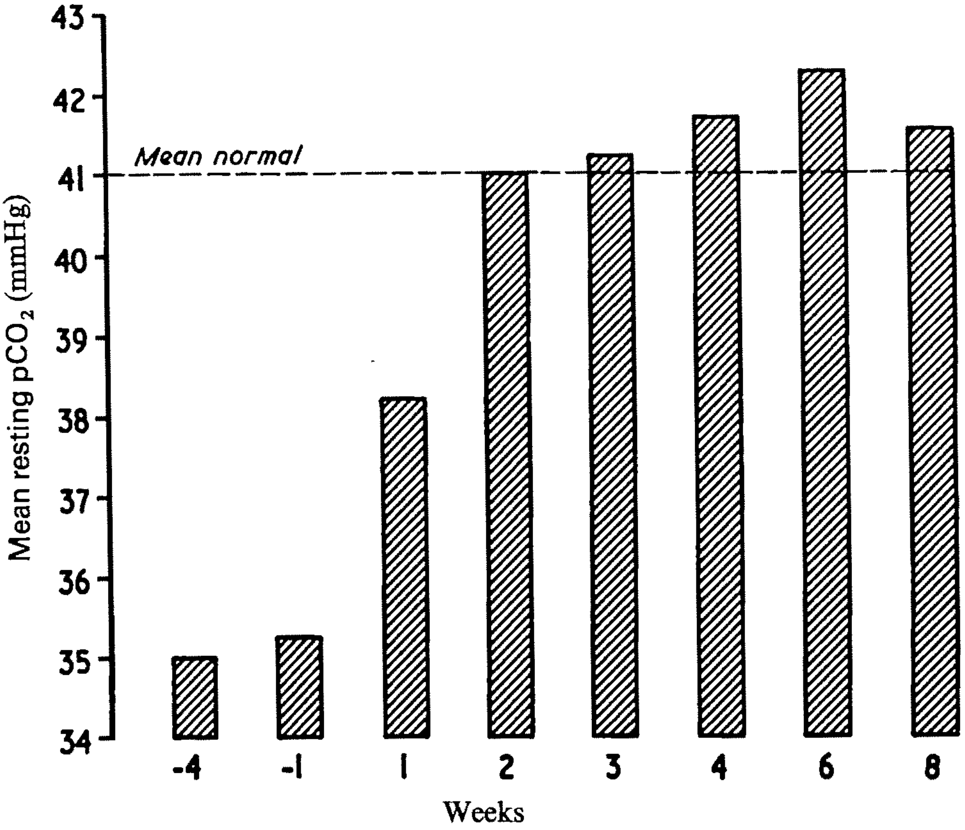


FIG. 2 Resting pCO_2 during baseline and treatment.

pCO_2 measure; all Pearson product-moment correlations gave a value of $r = 0.98$ or better. This stability of resting pCO_2 is further supported by the correlations between values on this occasion and the resting levels prior to the session five days later, values obtained being in the range $r = 0.87$ to $r = 0.91$. During this first session, the CO_2 levels immediately following the provocation test were measured to check whether the pCO_2 actually decreased appreciably. The mean resting level was 34.72 mmHg ($sd = 3.66$, $range = 31.4 - 42.5$); the mean change measured after provocation was -6.42 mmHg ($sd = 1.55$, $range = -4.46$ to -8.56). All subjects substantially increased their ventilation during the provocation test.

The week-by-week changes in pCO_2 levels during baseline and treatment phases are shown in Figure 2, together with a reference line indicating the mean level obtained from 23 normal subjects, matched for age and sex, whose resting pCO_2 was measured in the same way as the patients (mean $pCO_2 = 41.1$ mmHg, $sd = 2.63$). The resting levels of the patients were significantly lower than that of the matched controls ($t_1 = 5.57$, $P < 0.01$).

These results were subjected to a repeated measures analysis of variance, the comparison of interest being between baseline and respiratory treatment alone. A main effect of time was found ($P < 0.001$). Newman–Keuls tests were carried out, and showed no significant alteration of

pCO_2 during the baseline, and a significant increase above baseline by the end of the first week of respiratory control alone, which was sustained throughout this phase; pCO_2 at the second week of the second treatment phase was significantly higher than the first week of respiratory control alone (in all cases $P<0.05$). It is interesting to note that the levels of pCO_2 rise to the same level as those found in a non-patient sample.

Correlational analysis Correlations were calculated between outcome variables and pCO_2 before and during treatment. There was a significant negative correlation $r=-0.81$, $P<0.01$) between pre-treatment resting pCO_2 levels and ratings of the similarity between a brief period of overbreathing (provocation test) and symptoms experienced during panic attacks. Patients with a particularly low resting pCO_2 were therefore more likely to recognise symptoms of overbreathing as similar to their panic attacks. From inspection of the other correlations, it would appear that these two pre-treatment measures are closely related to change in outcome measures over the brief period of pure respiratory treatment. Similarity ratings correlated significantly with improvement in the M&M global problem rating ($r=0.81$, $P<0.01$), anxiety–depression rating ($r=0.66$, $P<0.05$), total avoidance score ($r=0.57$, $P<0.05$) and change in the BDI ($r=0.76$, $P<0.01$). A relationship between clinical outcome and success in reducing pCO_2 is indicated by the significant correlation ($r=0.65$, $P<0.05$) between improvement in the M&M global rating of distress and the change in pCO_2 at the end of the pure respiratory treatment. A related finding is the association between low pre-treatment resting pCO_2 levels and good clinical outcome following respiratory control (M&M Global Rating $r=-0.74$, $P<0.05$; Rating of General Anxiety $r=-0.62$, $P<0.05$). Change in pCO_2 following respiratory control treatment correlated with pretreatment resting pCO_2 ($r=-0.80$, $P<0.01$) and rating of similarity between panic attacks and the effects of the provocation test ($r=0.76$, $P<0.01$).

Discussion

Respiratory control treatment was associated with significant reductions in panic attack frequency and self-ratings of anxiety. Patients' initial resting pCO_2 levels were significantly lower than a group of age- and sex-matched controls, and increased to 'normal' levels during the course of treatment. It seems unlikely that these substantial improvements in clinical state could have occurred as a result of spontaneous remission, as we studied a chronic population (mean duration of current episode = 6.6 years), established a stable baseline, and then observed significant improvements from that baseline after a shorter period than the baseline (panic attack and frequency decreased and pCO_2 increased after only one week, which is 25% of the baseline). It therefore appears that the respiratory control package is an effective treatment for panic attacks. However, as the study did not include a control treatment, it is not possible to say which elements of the package are effective. In devising the treatment, it was assumed that the provision of a less catastrophic interpretation of patients' attacks and the provision of a technique for coping with these attacks would be important elements. The significant correlations between some measures of clinical improvement and the extent to which patients perceived the effects of overbreathing as similar to their panic attacks are consistent with this point of view. However, it could still be argued that non-specific treatment factors were crucially important.

The changes in panic attack frequency and fear questionnaire scores observed in the present study are very similar to those observed in our previous study (Clark *et al*, 1985) except that the respiratory treatment alone produced a reduction in the avoidance section of the Marks & Mathews Fear Questionnaire in the present study, but not in the previous study. This finding means that it could be argued that the improvement in clinical state may have occurred as a consequence of increased exposure to feared situations. However, all patients were specifically asked to refrain from going into situations that they had previously avoided. Under these conditions, it seems unlikely that increased exposure was an important therapeutic element. Perhaps a more plausible explanation of the change in avoidance score is that it is a consequence of the change in panic attack frequency and severity. Such a view would be consistent with the suggested central role of 'fear of fear' in the agoraphobic syndrome (Goldstein & Chambless, 1978). It would also explain why our previous study, which involved a shorter period of pure respiratory control, did not show changes in avoidance. Four weeks may have been too long a period to realistically expect patients not to try out their new found confidence by venturing into previously avoided situations.

A new feature of the present study was the inclusion of repeated measures of resting pCO_2. The finding that panic attack patients showed reduced resting levels of pCO_2 is consistent with the results of Lum (1976), who found a difference in resting pCO_2 between normals and a group of patients who experienced distressing bouts of physical symptoms, were referred to a cardiothoracic clinic, and were diagnosed as suffering from hyperventilation syndrome. In contrast to the present study and Lum (1976), Hardonk & Beumer (1979) reported that their hyperventilation syndrome patients had a normal resting pCO_2. However, Hardonk & Beumer placed strong diagnostic emphasis on the presence of tetanic symptoms. There is evidence that repeated overbreathing episodes decrease the likelihood of tetanic symptoms (Balke *et al*, 1958). It therefore appears that Hardonk & Beumer's diagnostic criteria excluded the very patients in whom reduced resting pCO_2 might be expected; that is, patients who persistently and repeatedly overbreathe over a long period with renal compensation for chronic alkalosis leading to a new pCO_2 'set point' in a similar fashion to that observed in adaptation to high altitudes (Gledhill *et al*, 1975). Clinically, the importance of the lowered resting pCO_2 observed in our patients lies in the fact that such a change in 'set point' is liable to increase the sensitivity of the physiological buffering system in a way that leads to enhanced responsiveness to even very small changes in pCO_2, such as those produced by psychological stressors and exercise (Okel & Hurst, 1961). Given this point, it is reassuring that respiratory control restored patients pCO_2 to normal levels, and so presumably reduced their previously heightened vulnerability to psychological stressors.

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*Paul M. Salkovskis, BSc. MPhil, ABPs.S. *Senior Clinical Psychologist, Department of Psychiatry, University of Oxford, Warneford Hospital, Oxford OX3 7JX.*

David R. O. Jones, BA, MSc, *Senior Clinical Pschologist, Department of Clinical Psychology, Torbay Health Authority, Belmont Court, Newton Road, Torquay.*

David M. Clark, MA, DPhil, *Lecturer in Psychology, Department of Psychiatry, University of Oxford, Warneford Hospital, Oxford. Fellow, Wolfson College, Oxford.*

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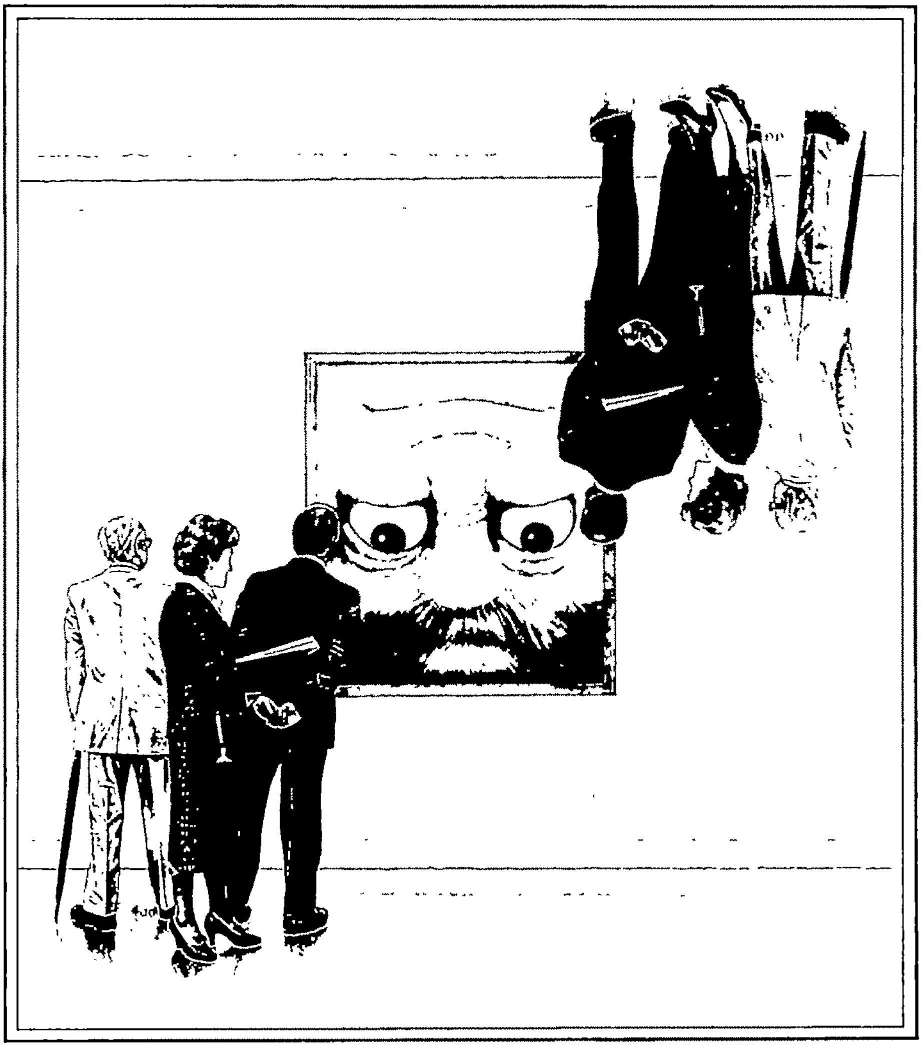

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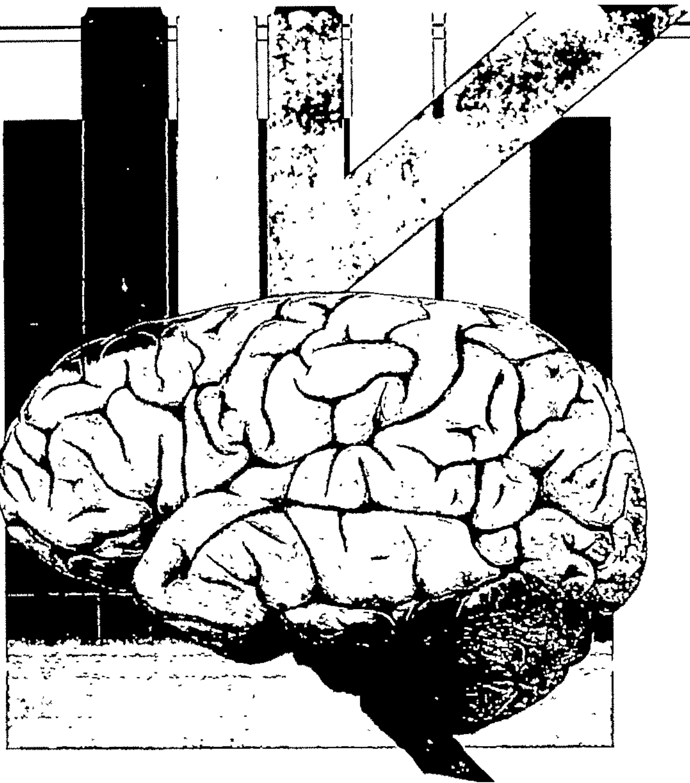

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At Risk Drinking among General Practice Attenders:
Prevalence, Characteristics and Alcohol-Related Problems

MICHAEL KING

In a sample of attenders screened at a London health centre, 13.6% of male and 1.3% of female respondents were drinking at levels considered unsafe by the Royal College of Psychiatrists, and yet revealed few indicators to alert the general practitioner in terms of classical alcohol-related disability. Males, the unemployed, and those of Scottish or Irish origin were over-represented in the 'at risk' group. A significant proportion viewed their general practitioner as a source of help.

At-risk drinking in the community may bear little relationship to hospital concepts of alcohol dependence, since the bulk of psychiatric morbidity presenting to general practitioners (GPs) fits poorly with classical psychiatric diagnosis (Shepherd *et al*, 1966; Goldberg & Huxley, 1980). Criteria of definition directly derived from community or primary care settings are therefore preferable for psychiatric epidemiological research (Ingham & Miller, 1976; Williams *et al*, 1980). Physical problems (Edwards & Grant, 1977: Smith, 1982), psychological problems (Ron, 1977, 1983; Parker & Noble, 1977, 1980; Goodwin & Erickson, 1979) and social problems (Edwards & Grant, 1977; Collins, 1982) associated with alcohol dependence both in the scientific and educational literature, are overwhelmingly based on clinic (secondary care) studies, and thus represent the severe end of a problem spectrum. Wilkins (1974), in a general practice survey of alcohol dependence, demonstrated that alcoholics tended to have a similar range of risk factors to those attending clinics, but his classification was based heavily on the conventional clinical view of alcohol dependence.

The aim of this study was to investigate the prevalence of at-risk drinking amongst attenders at a London primary care health centre, and to assess whether the problems traditionally associated with alcohol dependence occur in this group. The hypothesis was that at-risk drinkers in the community, in contrast to clinic alcoholics, are a hidden group, with few signs to alert the general practitioner. They may represent an early stage in a progression to alcoholism, and simple intervention by the GP might prove effective in halting this deterioration.

Method

Attenders at a West London health centre were screened for at-risk drinking (King, 1986) with the use of the CAGE questionnaire, which consists of the following four items:

1. *Have you ever felt you ought to cut down on your drinking?*
2. *Have people annoyed you by criticising your drinking?*
3. *Have you ever felt bad or guilty about your drinking?*
4. *Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover?*

This instrument has been shown to be effective in selecting at-risk drinkers from general or clinical populations at a cut-off point of two or more affirmative replies (Mayfield *et al*, 1974; Barrison *et al*, 1982; Bernadt *et al*, 1982). The health centre had five practitioners and one GP trainee for a practice population of approximately 10 000. Demographically, its area was similar to others in inner London, with a wide spread of social class, and a high percentage of flat accommodation, single households, and immigrant groups.

A representative series of surgeries was screened between June 1982 and March 1983. All attenders aged 16 years and over were asked to supply demographic details, answer two simple quantity-frequency questions about their usual consumption of alcohol, and complete the four CAGE questions. There was no attempt to disguise the nature of the survey.

All CAGE-positive respondents (two or more affirmative answers to the four CAGE questions), all CAGE-intermediate respondents (one affirmative reply), and a random selection of CAGE-negative respondents (all negative replies) were interviewed at home, where a complete drinking history for the year and the month prior to interview, and a survey of possible problems was undertaken.

Subjects were divided into five volume groups, and two variability groups following the method of Cahalan & Cisin (1968a, b), as follows:

Volume

Abstainers and infrequent drinkers: 0 to 0.14 drinks per day, i.e. up to one drink per week.
Low volume: more than 0.14, but less than or equal to 0.5 drinks per day.
Medium volume: more than 0.5, but less than or equal to three drinks per day.
High volume: more than three, but less than or equal to eight drinks per day.
At-risk: more than eight drinks per day.

Variability

Low maximum: never drank eight or more drinks on an occasion.
High maximum: drank eight or more drinks at least 'once in a while'.

Results

Of 451 attenders who were approached, 416 (92.2%) completed the questionnaire; five refused and 30 were unable to comply because of ill-health or illiteracy. A further nine questionnaires were incorrectly completed, leaving a total of 407 for analysis.

Table I details the demographic characteristics of the 407 subjects screened. The proportion of respondents who described themselves as unemployed seeking work was 5.6% of men and 7.4% of women, whereas rates for the local borough over the period of data collection ranged from 15.7 to 16.7% for men and 7.5 to 7.9% for women.

Numbers of subjects successfully interviewed in each CAGE grouping are shown in Table II, and the relationship of alcohol consumption to original CAGE grouping in Table III.

The definition of a case was based on the guidelines of the Royal College of Psychiatrists (1979), where consumption of more than eight drinks per day is considered unsafe. One drink is defined as one half-pint of beer, a single measure of spirits, one 4-oz glass of table wine, or one small glass of fortified wine.

Respondents consuming more than eight drinks daily constituted 13.6% of males, 1.3% of females, or 5.0% overall. Those drinking at levels greater than *twice* the College upper limit of 16 drinks per day comprised 8.7% of males, 0.9% of females, or 3.3% overall. When a cut-off point of over five drinks daily was considered, the upper limit of safety recommended for women by the Health Education Council, 27.6% of males (confidence limits ± 6%), 3.7% of females, or 11.5% overall, were consuming in excess of this amount. The figure for males is less

TABLE I
Demographic characteristics of the screened population

	n	%
Sex		
male	121	(30)
female	285	(70)
Age		
16–45 years	268	(67)
over 45 years	133	(33)
Marital status		
Never married	149	(37)
Ever married	249	(63)
Education		
Age at leaving full-time education		
≤16 years	176	(48)
>16 years	189	(52)
Social class		
I	13	(3)
II	81	(20)
III	99	(24)
IV	26	(6)
V	9	(2)
Student	18	(4)
Housewife	75	(18)
Retired	42	(10)
Unemployed	25	(6)
Not known	19	(5)
Country of birth		
Ireland	49	(12)
Scotland	11	(3)
England/Wales	231	(57)
Other	114	(28)

TABLE II
Breakdown of subjects interviewed in each CAGE group

	CAGE-negative	*CAGE-intermediate*	*CAGE-positive*	*Total*
Number	318	51	38	407
Number selected for interview	34	51	38	117
Number actually interviewed	31	46	31	108

TABLE III
Volume categories for each CAGE group

Volume category	*CAGE-negative*		*CAGE-intermediate*		*CAGE-positive*	
	M	*F*	*M*	*F*	*M*	*F*
Abstainers	3	7	0	2	0	2
Low volume	3	4	1	3	0	0
Medium volume	2	7	6	13	1	5
High volume	3	2	6	12	5	4
At risk	0	0	2	1	12	2

M = male, F = female.

TABLE IV
Volume groups compared with each other and the remainder of the population not interviewed

	Not interviewed	*Abstained/ Low*	*Medium volume*	*High volume*	*At risk*
Sex					
Male	77 (26)	7 (28)	9 (26)	14 (44)	14 (82)
Female	221 (74)	18 (72)	25 (74)	18 (56)	3 (18)
Employed					
Unemployed	11 (4)	3 (9)	3 (9)	4 (13)	4 (25)
Other	273 (96)	21 (91)	31 (91)	27 (87)	12 (75)
Country of birth					
Irish	33 (11)	4 (17)	5 (15)	2 (6)	5 (29)
Scottish	5 (2)	0	2 (6)	2 (6)	2 (12)
English/Welsh	166 (56)	13 (54)	23 (68)	21 (66)	8 (47)
Other	94 (32)	7 (29)	4 (12)	7 (22)	2 (12)

Figures in parentheses = cell %.

precise, as one male in the CAGE-negative group was drinking at this level, but only 11 out of the 82 CAGE-negative males were interviewed.

Reported changes of alcohol consumption in the month prior to interview were negligible in the CAGE-negative and intermediate groupings. However, there was considerable change in the CAGE-positive group: 58% of subjects reported some change in this month, and a reduced total of 12 persons at risk resulted. At-risk consumption for *either* the year *or* the month before interview, was reported by 15.5% of males, 1.8% of females, or 5.9% overall.

King (1986) showed that the CAGE performed well as a screening instrument to detect current at-risk drinking in this population of GP attenders, with a sensitivity of 84%, specificity of 95%, and a positive predictive value of 45%.

Responses to the simple quantity-frequency questions on the screening form were often inaccurate. Of 349 respondents who answered clearly enough to be analysed, only one reported consumption in the at-risk range.

Drinking categories

Volume groups: When the at-risk group was compared with the remainder of the screened population (Table IV), there were significantly more males ($P<0.001$), unemployed ($P<0.02$), Irish ($P<0.05$), and Scots ($P<0.02$) amongst the former.

CAGE groups: A similar pattern emerges when CAGE groupings are compared with each other, with more males ($P<0.001$), unemployed ($P<0.05$), and Irish and Scots ($P<0.01$) amongst CAGE positive respondents (Table V). An analysis of variance was performed on CAGE groupings, from which sex of the respondent emerged as the only independent variable ($P<0.02$).

Variability groups: All at-risk subjects, by definition, were high maximum consumers (eight or more drinks on an

TABLE V
Comparison of CAGE groups

	CAGE-negative	*CAGE-intermediate*	*CAGE-positive*	*Significance*
Male	82 (26)	18 (35)	21 (55)	$P<0.001$
Female	235 (74)	33 (65)	17 (45)	
Unemployed	14 (5)	6 (12)	5 (14)	$P<0.05$
All others	290 (95)	43 (88)	31 (86)	
Irish/Scots	39 (12)	8 (16)	13 (34)	$P<0.005$
All others	278 (88)	42 (84)	25 (66)	

Figures in parentheses = cell %.

occasion at least 'once in a while'). However, high maximum consumers, drinking at lower volumes, broadly resembled those at risk in having significantly more males ($P<0.03$), unemployed ($P<0.05$), and Scots ($P<0.001$) in their midst, but they were also significantly younger ($P<0.02$).

Almost 30% of CAGE-negative respondents were high maximum consumers, but none were at risk.

Low maximum consumers (never consuming eight or more drinks on an occasion) showed no differences on demographic characteristics from the total population screened.

There were insufficient numbers to use the full breakdown into the nine possible volume-variability groups.

Alcohol-related disability

There was no significant correlation of volume or variability grouping with absenteeism from work, accidents at home or work, road traffic accidents, general or psychiatric hospital contact, or use of psychotropic drugs.

Approach to general practitioner

Five out of the 17 at-risk drinkers (29.4%), three high-volume (9.3%), and one abstainer/infrequent drinker, reported that they had approached their GP because of a concern about drinking.

Discussion

It must be emphasised that no attempt was made to establish the presence of physical dependence on alcohol, the aim being to investigate the broader picture of at-risk drinking. Figures quoted here for alcohol consumption are clearly dependent on the accuracy of self-reports, which although subject to distortion (Uchalick, 1979; Plant 1979; Chick *et al*, 1981), have been found overall to be acceptably valid and reliable (McCrady *et al*, 1978; Maisto *et al*, 1979, 1982).

Refusal of interview may have been due to defensiveness about the topic. Those in the CAGE-positive group who refused interview or who were unobtainable, were predominantly people who appeared to have alcohol problems (either from screening quantity-frequency replies, or from practice information). By implication, those who refused to take part in the initial screening may also have been biased in the direction of heavier consumption, although this number was very small.

Characteristics of the study population

The screened sample differed from figures for general practice attenders (Royal College of General Practitioners, 1979) for the south of England by containing fewer males than expected. There were also fewer unemployed among the attenders (especially males) than for the local borough during the period of data collection. This is surprising in the face of other work suggesting that the unemployed make greater demands on medical services (Tischler *et al*, 1975; Farrow, 1983).

Patterns of consumption

The discussion will concentrate on reported consumption over the year prior to interview. Comparison with other studies is difficult, due to varying concepts of alcohol abuse. Prevalence figures for this study are higher than several other general practice surveys (Wilkins, 1974; Buchan *et al*, 1981): Patterson (1972) derived a closely similar rate to the current study (52.0 per 1000), and Baxter *et al* (1980) considered that 25% of 202 consecutive volunteers among attenders in London were 'likely' excessive drinkers, in what is the highest prevalence ever reported from general practice. Studies of excessive drinking in the community have generally reported prevalences similar to, or *higher* than the highest levels reported from general practice (Edwards *et al*, 1972a; Cartwright *et al*, 1978; Plant & Pirie, 1979). This is in contrast to almost all studies of physical or psychiatric morbidity, which report higher prevalences among subjects presenting in primary care than in the community (Goldberg & Huxley, 1980). It may be that the early studies were based on the poor records and/or unreliable memories of the doctors, or, less plausibly, that at-risk drinkers are less likely than others in the community to attend their GP.

At-risk drinking

Sex Sex was the only independent variable, with males more likely to be at-risk drinkers than females ($P<0.0001$), but when lower daily volumes are considered, differences between the sexes diminish. The ratio of 10 men to 1 woman, in the *at-risk* category, drops to 2 to 1 in the *high-volume* group, where individuals were consuming between three and eight drinks daily. The *medium-volume* group contained approximately equal proportions of men and women.

All surveys, be they in a special population, general practice, or the community, reveal higher rates of alcohol dependence for men than for women. This difference is linked to socio-cultural patterns of drinking, but almost certainly also, to the greater social stigma applied to drinking women, which will act to increase their denial of heavy consumption (Royal College of Psychiatrists, 1979). Women may less readily admit to a drinking problem, but unfortunately are placed at greater risk of cirrhotic damage for lower levels of consumption than men (Williams & Davis, 1977). For at-risk drinking, the ratio here of 10 men to 1 woman is in keeping with earlier estimates (Edwards *et al*, 1972a; Cartwright *et al*, 1978), but not with more recent surveys, which have reported increasing levels of consumption by women (Royal College of Psychiatrists, 1979; Chick, 1982; Plant *et al*, 1982). Rates of convictions for drunkenness, alcohol-related hospital admissions, and mortality are also rising for women (Smith, 1982). This trend is seen in the current study, albeit at levels of consumption below the at-risk cut-off point of eight drinks daily. In the high and medium-volume groupings, women were drinking at levels comparable with men. It is increasingly recognised, however, that lower safety limits suggested by organisations such as the Health Education Council may be more appropriate for women. These results would therefore indicate that although women may be drinking at somewhat lower levels than men, they are placed at equal risk for damage.

Employment Significantly more at-risk drinkers were unemployed, despite a low proportion of the unemployed in the screened population.

Periods of economic recession and unemployment have been linked by some with increased alcohol-related hospital admissions (Brenner, 1973), although others have disagreed (Gravelle *et al*, 1981). Threatened redundancy has been linked to heavy drinking (Jenkins *et al*, 1982), although in this study, no clear previous levels of consumption were recorded. Rees (1984) considered that there were no direct links between unemployment and heavy drinking and that the picture was complicated by individual vulnerability and personal circumstances. Although sickness, lateness, and absenteeism, as well as reduced performance whilst at work, are claimed associations with *clinical alcoholism* (Observer & Maxwell, 1959; Edwards *et al*, 1967; Smith, 1982) and are likely to predispose an individual to dismissal, at-risk drinkers in the community may be less impaired, and thus less vulnerable. Heavy drinking might therefore be a result of unemployment rather than a cause.

Country of birth Significantly more Irish and Scots were found amongst the at-risk drinkers, and high maximum male consumers were also more likely to be Scottish.

Dight (1976), Saunders & Kershaw (1978), and Plant & Pirie (1979) reported higher rates of alcoholism in Scotland than the rest of Britain. Wilson (1980), however, in a comparison of surveys, could not support this, and Latcham *et al* (1984) and Crawford *et al* (1984), in a direct comparison between areas in Scotland and southern England, found no appreciable differences between the regions.

Walsh (1969) showed that Ireland in 1964 had the highest national first admission rates for alcoholism in Europe, exceeded only by France, but this was not supported by Wilson (1980). An excess of alcoholism has been reported among Irish and Scots living in England, compared to other immigrant groups (Edwards *et al*, 1968; Bagley & Binitie, 1970), but Irish immigrants, at least, were not found to be predisposed to, or to suffer increased alcoholism as a result of immigration *per se* (Clare 1972). It is important that general practitioners in London should be alert to the higher incidence of at-risk drinking in these two migrant groups.

Other associations

Age Although age was not a significant factor amongst at-risk drinkers, high maximum consumers included significantly more individuals under the age of 45 years. Chick (1982) claimed that in all surveys in the UK and Scandinavia in the past 15 years, men in their early 20s have been the heaviest consumers; this trend has been supported by others (Plant *et al,* 1982). It seems, however, that many such individuals reduce consumption as they get older (Fillimore, 1974), and it may well be that social factors determine age-related patterns of alcohol consumption. Unfortunately, this period of heavy drinking is not harmless, but is attended by a range of problems (Edwards *et al,* 1972b; Plant *et al,* 1982) and increasing rates of treatment for alcoholism in the young (Gomberg, 1982).

Social class Social class was not a significant factor for either at-risk, or high-maximum drinking; this confirms recent reports of lessening social class differences in alcohol consumption. Edwards *et al* (1972b) noted from a survey of an inner London suburb in 1965, that members of social classes I and II drank more, both in terms of quantity and frequency, than other groups. However, Cartwright *et al* (1978), reporting from the same area 9 years later, found the differences to be much less marked. Plant & Pirie (1979) suggested that alcohol consumption by members of social classes IV and V may be starting to exceed the others, but this was not the case here.

Alcohol-related problems

The overwhelming conclusion, for this general practice sample, was that there were few associations between at-risk drinking and problems recorded.

Much investigation in this area has dealt with chronic alcoholics who are severely impaired, and therefore more likely to be disabled; in fact, such disabilities may be instrumental in establishing them in treatment in the first place. Heavy drinkers in the community appear to be a less visible group who, while consuming possibly damaging amounts of alcohol, remain in equilibrium with their social circumstances. Disabilities such as alcohol-related accidents, poor work performance, and psychiatric or medical problems, may not come to the notice of the GP.

Therefore, to rely on the alcohol-related disabilities that are frequently quoted as indicators of heavy drinking for the general population (Wilkins, 1974; Bligh, 1984) may be to miss a large proportion of those abusing alcohol (Clare & King, 1983). It might be argued that at-risk drinkers detected here were mild cases, inappropriately labelled as people abusing alcohol, but most of them were drinking well in excess of eight drinks per day—a generous cut-off point—and more than half were taking in excess of 16 drinks daily.

Contact with the general practitioner

Of considerable importance is that almost 30% of individuals claimed to have approached the GP for help with their excessive drinking, but other work has shown that alcoholics, variously defined, are less eager to approach their GP (Moss & Davies, 1967; Edwards *et al,* 1973; Wilkins, 1974). Sampling general practice attenders in the manner of this study will, of necessity, bias the result towards people who consult their doctor more readily, but despite this limitation, it seems that a considerable proportion of at-risk drinkers increasingly regard the GP as a source of help.

Implications for further research

The next logical step in the study of at-risk drinking is a controlled assessment of simple intervention by the GP along the lines for cigarette smoking (Russell *et al,* 1979), where it was found that simple advice motivated considerably more people to give up. Although excessive alcohol consumption in the community presents with few indicators to alert the GP, intervention at this point could be crucial. Accurate information is needed about the efficacy of treatment for at-risk drinking at the level of primary care. Even small gains could represent an enormous advance, in terms of numbers of people helped, on those in current programmes at hospital-based clinics. The CAGE has been shown to be a valid and reliable instrument (King, 1986) and is currently in use in such an intervention study in London (Wallace & Haines, 1985).

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Michael B. King, BSc, MBChB, MRCP, MRCGP, MRCPsych, *Honorary Lecturer, General Practice Research Unit, Institute of Psychiatry, and Honorary Clinical Senior Registrar, Maudsley Hospital, London SE5.*

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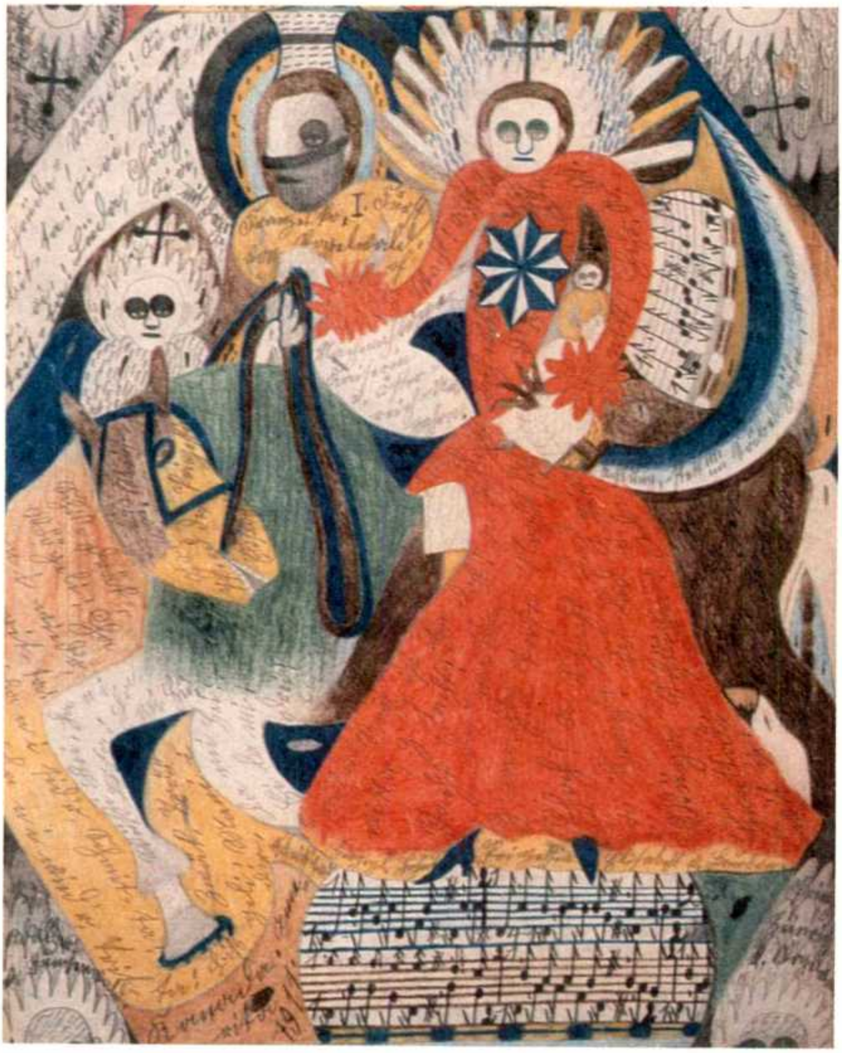

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Depression Influences Intellectual Impairment in Stroke Patients

ROBERT G. ROBINSON, KAREN BOLLA-WILSON, EDITH KAPLAN, JOHN R. LIPSEY and THOMAS R. PRICE

Patients with ischaemic lesions of the left cerebral hemisphere were examined for depression and intellectual impairment: in non-depressed patients, the severity of impairment was related to both lesion volume and location, as assessed by CT scan analysis. Cognitive impairment in patients with major depression was greater than predicted by lesion volume alone, and when patients were matched for severity of impairment, depressed patients had smaller lesion volumes than the non-depressed. After six months, non-depressed patients had significantly less cognitive impairment than depressed patients who showed no improvement. Both depression and lesion volume were significantly and independently related to cognitive impairment. These findings suggest that post-stroke depression can produce a true dementia in its own right, and that treatment of post-stroke depression might benefit cognitive function.

For more than 20 years, clinicians have recognised that reversible dementia can be associated with a variety of functional psychiatric disorders, particularly depression. The term 'pseudo-dementia' has been applied to this disorder, and was used primarily because of the reversible nature of the dementia (Caine, 1981; Kiloh, 1961; Nott & Fleminger, 1975; Wells, 1979). McHugh & Folstein (1979) and Caine (1981) noted the characteristic symptoms of lack of motivation and drive, difficulty with verbal elaboration, poor memory retrieval, and the improvement of performance with prodding. Based on the existence of these symptoms, which are also associated with subcortical brain injury, they suggested that the dementia associated with depression may be related to subcortical and perhaps biogenic amine mechanisms.

Caine (1981) has suggested that the diagnosis of 'pseudo-dementia' be based on four criteria: (1) intellectual impairment with a primary psychiatric disorder, (2) features of neuropsychological abnormality resembling neuropathologically induced intellectual deficit, (3) reversibility of intellectual disorder and (4) no apparent primary neuropathological process. It might be possible, however, that a depressive disorder provoked by a neuropathological process, such as that following stroke, could produce a 'pseudo-dementia'.

For several years, we have been examining mood disorders in stroke patients (Lipsey *et al*, 1983; Robinson & Benson, 1981; Robinson & Szetela, 1981; Robinson & Price, 1982; Robinson *et al*, 1983a,b, 1984a,b,c) and have reported that patients with left frontal brain injury are more frequently and more severely depressed than those with lesions in other areas (Robinson *et al*, 1984a,c). In several groups of such patients, we have also demonstrated a consistent, positive correlation between the proximity of the lesion to the frontal pole, as visualised on CT scan, and the severity of depression (Robinson & Szetela, 1981; Robinson *et al*, 1983a; Robinson *et al*, 1984a,c). In addition to finding a strong relationship between the anatomical locus of the lesion and the severity of depression, we have found a weaker—although significant relationship between the severity of depression and severity of intellectual impairment (Robinson *et al*, 1983b; Robinson *et al*, 1984c). Although it has generally been assumed that the physical and intellectual impairments associated with stroke are the cause of the depressive disorder (Benson, 1973; Charatan & Fisk, 1978), the findings of several investigations have raised doubt about this assumption (Finkelstein *et al*, 1982; Folstein *et al*, 1977; Robinson & Szetela, 1981; Ross & Rush, 1981). In fact, it is possible that the depressive disorder might contribute to the intellectual or perhaps physical impairment rather than the converse.

In the present study, we examined the relationship between intellectual deficit and post-stroke depression. In our view, the data suggest that both the depression and neuropathological lesion contribute to the development and severity of intellectual impairment in these patients.

Method

Patient population

A consecutive series of 184 patients admitted to the University of Maryland Hospital with acute thromboembolic stroke (N = 144) or intracerebral haemorrhage (N = 40) were screened. Of these, 53 could not be interviewed because of decreased level of consciousness or severe comprehension deficits, seven were discharged before they could be examined, and one refused interview. Of the 123 who were examined, patients with previous history of stroke or other brain injury or CT scan evidence of prior brain injury were excluded, and only those 38 who had clinical and/or CT scan evidence consistent with a single lesion of the left hemisphere were evaluated.

Neurological evaluation

The neurological examination and diagnosis was done (TRP) in accordance with the examination and diagnostic criteria utilised by the NINCDS Pilot Stroke Data Bank (Kunitz *et al*, 1984).

Computerised tomography (CT) scans were done within three days of hospital admission, as part of the patient's clinical care. Readings of CT scans were by a neuroradiologist who was blind to the psychiatric or cognitive findings. The anterior location of each lesion (expressed as a percentage of total AP distance) was defined as the mean distance of the anterior border of the lesion from the frontal pole, for all slices in which the lesion was visible. The posterior location of the lesion was defined as the mean distance of the posterior border from the frontal pole. Lesion volume (expressed as percentage of total brain volume) was calculated from the ratio of the largest cross-sectional area of the lesion on any CT slice, divided by the largest cross-sectional area of total brain on a CT slice passing through the lateral ventricles. Lesion and total brain areas were determined by a computerised area calculation programme, using an electronic cursor. Although we have previously used a procedure based on nine consecutive dorsal slices and direct volume calculations (Robinson & Szetela, 1981; Robinson *et al*, 1984a), this new abbreviated method gave volume measurements which correlated strongly with volume measurements using the prior method ($r = 0.94$ for 20 randomly selected scans).

Psychiatric evaluation

After obtaining informed consent, patients were given a series of standardised quantifiable measures of mood and physical impairment, between 11 am and 2 pm, to minimise any possible effect of diurnal mood variation. The Hamilton Depression Scale (Hamilton, 1960) (17-item questionnaire) was completed. The Zung Depression Scale (Zung, 1965) (a 20-question self-rated questionnaire) was read to each patient, and their responses scored. A modified Present State Examination (PSE) (Wing *et al*, 1974) which has been described by Robinson *et al* (1983a) was also administered.

Diagnosis of depression was based on DSM III criteria (American Psychiatric Association, 1980) using the symptoms elicited by the PSE. The method used for conversion from PSE symptoms to DSM III diagnostic criteria has been discussed by Robinson *et al* (1983a) and is available on request.

Although all patients had brain injury, and therefore did not meet strict criteria for DSM III diagnosis of either major or minor (dysthymic) depression, we have separated major from minor depression because the former is specifically associated with left anterior lesions, while the latter most commonly occurs with left posterior lesions (Robinson *et al*, 1984a). In addition, we have shown previously (Robinson *et al*, 1984b) that, using the above scales, diagnosis by DSM III symptom criteria produces groups with statistically significant differences in mean depression scores.

The Johns Hopkins Functioning Inventory (JHFI) (Robinson & Benson, 1981; Robinson & Szetela, 1981) (a ten-item questionnaire), which evaluates the patient's degree of independence in activities of daily living such as walking, dressing, and eating was scored by the examiner and a nurse who knew the patient well. Scores may range from 0 to 27, with higher scores indicating more severe impairment.

Cognitive evaluation

All patients were administered the Mini-Mental State Examination (MMSE) (Folstein *et al*, 1975)—an 11-item examination, found to be reliable and valid in assessing cognitive function in a vareity of states including dementia and brain injury (McHugh & Folstein, 1979). Scores may range from 0 to 30, 23 or below indicating significant cognitive impairment. By the time we examine patients in hospital, their cognitive impairment is quite stable at one week, three months, and six months follow-up (Robinson *et al*, 1985).

Statistical analysis

Inter-group comparisons of parametric data used means, standard deviations, t-tests, analysis of variance, Pearson correlation coefficients, and multiple linear regression analysis. Frequency distributions were compared using chi-square tests (with the Yates modification as appropriate for small cell size).

Results

Study population

Background characteristics of the 38 patients, grouped by diagnosis, are shown in Table I: patients were predominantly in their 50s and 60s, black, lower socio-economic class (Hollingshead Class IV or V), male, and were generally

TABLE I
Characteristics of study population

	Major depression (n=11)	*Minor depression (n=10)*	*No depression (n=17)*
Demographics			
Age (years)	51±16	55±10	61±11
Sex ratio (M/F)	5/6	8/2	11/6
Race (bl/wh)	7/4	7/3	10/7
Marital status (married/other)	5/6	8/2	9/8
Socioeconomic status (Hollingshead class IV or V/class I–III)	10/1	9/1	11/6
Education (years)	9.8±2.4	9.5±3.4	10.3±2.7
Time since stroke (days)	13±10	9±5	10±6
Hx of alcohol abuse (neg/pos)	9/2	9/1	16/1
Handedness (R/L or mixed)[a]	7/4	10/0	17/0
Examination scores			
Zung score	61.9±8.1*	44.8±9.1†	35.5±7.1
Hamilton score	14.6±6.1*	6.8±2.9†	3.3±1.8
Total PSE score	26.2±7.6*	10.9±4.9†	4.0±3.3
Mini-Mental score	13.0±5.8*	25.0±4.5	22.0±6.0
JHFI score	11.2±8.2*	5.9±5.9	5.3±3.9

Values given are frequencies or means ± SD.
[a] Significantly different than a random distribution.
$X^2_{\text{Yates}} = 7.7$, df = 2, $P < 0.025$.
*,†Significantly different than the other two groups by t-test, $P < 0.05$.

TABLE II
Neurological findings and history (number of finding in parenthesis)

	Major depression (n=11)	*Minor depression (n=10)*	*No depression (n=17)*
Hemiparesis	91% (10)	70% (7)	88% (15)
Sensory deficit	36% (4)	20% (2)	41% (7)
Visual field loss	27% (3)	10% (1)	12% (2)
Aphasia (total)	34% (4)	20% (2)	47% (8)
Broca	(2)	(1)	(4)
Wernicke		(1)	(3)
Other	(2)		(1)
Ischaemic infarct	64% (7)	80% (8)	82% (14)
Intraparenchymal haemorrhage	36% (4)	20% (2)	18% (3)
Cortical/subcortical (based on CT scan and/or clinical localisation)	73%/27% (8/3)	60%/40% (6/4)	82%/18% (14/3)

examined within two weeks of their stroke (range two to 52 days). The only inter-group difference was that a significantly greater number of patients with major depression were left-handed, as compared to patients with minor depression or no depression.

Neurological findings

The neurological findings of the study population, separated by psychiatric diagnosis, are shown in Table II. Slightly more than 75% of the patients had ischaemic infarcts, while the remainder had intracerebral haemorrhages: approximately 75% of the lesions were cortical, with or without sub-cortical involvement, and the rest exclusively sub-cortical. All patients had left-hemisphere infarcts, and most of them were hemiparetic; approximately 34% had a hemisensory deficit, and almost 40% an aphasia. There were no significant differences in the neurological diagnoses or findings between any of the diagnostic groups (Table II).

Psychiatric findings

Patients with major depression had significantly higher mean depression scores and JHFI scores and significantly lower mean Mini-Mental Scores than the other two groups (Table I). In addition, mean depression scores were significantly higher in the minor depression group, compared with the no-depression group, although these two groups did not differ in their mean Mini-Mental or JHFI scores.

Relationship between psychiatric diagnosis and intellectual impairment

The number of patients with abnormal mini-mental scores (i.e. less than 23) in each diagnostic category are shown in Table III. *All* patients with major depression had abnormal Mini-Mental scores, while less than half those with either minor depression or no depression had abnormal scores.

Relationship between intellectual impairment and lesion size and location

Of the 38 subjects, 29 had CT scan evidence of a single left hemisphere lesion, while nine had negative CT scans, despite clear and persistent neurological findings indicative of left hemisphere brain injury and a neurological diagnosis of left-hemisphere stroke. The fact that nine of the patients' lesions were not visualised on CT scan is not unusual, since the lesion may have been too small to see, or the tissue changes necessary to produce the density contrast on CT scan were still evolving during the first few weeks after stroke.

The anterior-posterior location of the lesion was not significantly different between the patients with abnormal Mini-Mental scores and those with normal Mini-Mental scores (Table III). However, the size of the lesion was significantly greater in patients with abnormal Mini-Mental scores as compared to those with normal scores.

When the lesion size was examined in relation to intellectual impairment, patients without depression were found to have a highly significant negative correlation between lesion size and Mini-Mental score (Fig. 1); i.e. the larger the lesion size, the greater the intellectual deficit ($r = -0.73, P < 0.01$). Cognitive impairment in patients with major depression also showed a significant correlation with lesion volume ($r = -0.63$, df$=8$, $P < 0.05$), although their Mini-Mental scores for equal lesion volumes tended to be

TABLE III

Relationship of intellectual impairment to diagnosis, lesion size, or location

*Diagnosis**	*Abnormal mini-mental (n=20)*	*Normal mini-mental (n=18)*
Major depression	11	0
Minor depression	2	8
None	7	10
Lesion measurement	(*n*=18)‡	(*n*=11)‡
Lesion size		
(% of brain volume)	9.5±7.0†	4.7±5.1
Lesion location		
(% of A-P distance)	38.9±18.7	34.1±14.3

Values given are frequencies or means ± SD.

*Significantly different than a random distribution, $X^2 = 15.3$, df$=2$, $P < 0.001$.

†Significantly greater than normal Mini-Mental score group, $t = 2.0$, df$=27$, $P < 0.05$.

‡Nine patients did not have a lesion that was demonstrable by CT scan.

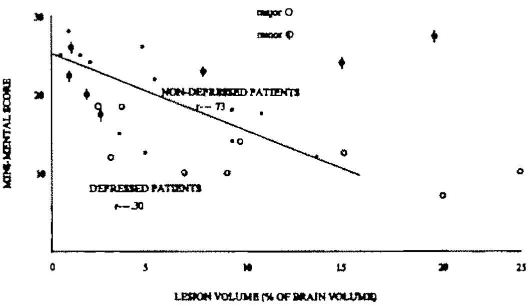

FIG. 1. Mini-Mental score and brain lesion volume as measured from CT scan were found to have a linear relationship and significant correlation ($P < 0.01$) for *non-depressed* (solid circles) patients. Larger lesion volumes produced greater degrees of cognitive impairment. Although Mini-Mental score correlated significantly with lesion volume in patients with major depression (open circles) cognitive impairment did not correlate significantly with lesion volume in patients with minor depression (crossed circle) or in the overall group of depressed patients (major plus minor). Correlation coefficients are shown on the figure.

lower than the non-depressed patients. Lesion volumes did not significantly correlate with Mini-Mental score in the patients with minor depression ($r=0.50$, df$=6$, P—NS).

There was also a significant relationship between lesion location and intellectual impairment in those patients with no depression; i.e. the *posterior* border of the lesion was significantly correlated with the severity of the intellectual impairment in patients with no depression ($r=-0.59$, $P<0.05$). Although we have generally correlated the *anterior* border of the lesion with depression score (Lipsey *et al*, 1983; Robinson & Szetela, 1981; Robinson *et al*, 1984a), we found in this instance that the correlation between the posterior border of the lesion and the Mini-Mental score (i.e. $r=-0.59$) was greater than the correlation between the anterior border and Mini-Mental score (i.e. $r=-0.35$). Cognitive impairment was also found to correlate with posterior border of the lesion in patients with major depression ($r=-0.78$, df$=8$, $P<0.05$), but not in patients with minor depression ($r=-0.18$, df$=6$, P—*NS*).

There were ten patients who had purely sub-cortical lesions by CT Scan analysis. When these were divided into the ones with abnormal ($n=5$) and normal Mini-Mental scores ($n=5$), the patients with abnormal scores were found to be significantly more depressed (PSE 19.8 ± 8.1 SD abnl vs. 4.0 ± 3.2 SD nl, $t=4.1$, df$=8$, $P<0.01$; Hamilton 10.4 ± 2.30 SD abnl vs. 4.1 ± 2.7 SD nl, $t=4.0$, df$=8$, $P<0.01$; Zung 57.2 ± 5.7 SD abnl vs. 37.2 ± 5.7 SD nl $t=5.5$ df$=8$, $P<0.01$). The functional physical impairment—as measured by the JHFI—was not, however, significantly different between the two groups (9.0 ± 7.3 SD abnl vs. 8.6 ± 2.7 SD nl, $t=0.1$, df$=8$, P=*NS*).

A multiple linear regression analysis was done for the entire group of patients, using Mini-Mental scores as the dependent variable, and lesion size and severity of depression as the independent variables. The multiple correlation coefficient was $R=0.700$, df$=2{,}24$ $P<0.005$; the partial regression coefficient for Hamilton depression score, and Mini-Mental score was -0.555 ($t=3.20$, df$=24$ $P<0.01$), and the partial regression coefficient for lesion size and Mini-Mental score was -0.417 ($t=3.06$, df$=24$ $P<0.01$). There was, however, no significant correlation between Hamilton depression score and lesion size ($r=0.015$, df$=24$ P—*NS*), suggesting that depression and lesion size both independently contribute to intellectual impairment. We also compared depressed and non-depressed patients for lesion size, when we controlled for level of intellectual impairment. Patients with and without depression ($n=10$ per group) were blindly matched for Mini-Mental score (mean 19.0 ± 5.7 SD). Patients with depression had significantly smaller lesion volumes (3.3 ± 2.7 SD) than non-depressed patients (6.2 ± 4.0 SD) ($t=1.9$, df$=18$ P one tail <0.05). The JHFI scores in the two groups, however, were not significantly different (7.8 ± 6.7 SD depressed, 6.9 ± 3.9 SD non-depressed).

Relationship of depression to longitudinal course of intellectual impairment

As part of our longitudinal study of stroke patients Robinson *et al*, 1983b, 1984b,c), we repeated Mini-Mental examinations at six months post-stroke for eight of the non-depressed patients who remained so throughout the six-month period, and for nine of those with major or minor depression who remained depressed throughout the six-month period. Repeated measures analysis of variance demonstrated that the depressed patients had significantly lower Mini-Mental scores (greater cognitive impairment) than non-depressed patients ($F(1,15)=7.0$, $P<0.025$). In addition, although the depressed patients were slightly (non-significantly) lower in their scores at the time of the initial evaluation compared to the non-depressed, at six months there was an improvement in the Mini-Mental scores in the non-depressed group (23.2 ± 5.2→26.1 ± 4.5), while the depressed group showed a slight decline (21.8 ± 5.4→19.7 ± 5.3). By the end of the six-month period, Mini-Mental scores of the depressed patients were significantly lower by t-test than those of the non-depressed ($t=2.7$, $P<0.02$). During this follow-up period, only one in-patient with depression spontaneously improved by six months follow-up. This patient's Mini-Mental score improved during this time from 17 to 20.

Discussion

This study has demonstrated that more than 50% of stroke patients, selected only for having a single left-hemisphere lesion, had significant intellectual impairment as measured by the Mini-Mental State Examination. The prevalence of intellectual impairment, however, was associated with the severity of depression; i.e. all patients with major depression, but just over 40% of the non-depressed patients, were found to have intellectual impairment. Patients with intellectual impairment were found to differ from non-impaired patients by having larger lesion volumes. Non-depressed patients had a highly significant correlation between lesion size and severity of intellectual impairment, and also between the posterior border of the lesion and the severity of intellectual impairment. Patients with major depression, however, had greater cognitive impairment for comparable lesion size, and when cognitive impairment was held constant, depressed patients had significantly smaller lesion size than non-depressed patients. In addition, both lesion size and depression were found to relate independently to intellectual impairment. Over the course of a six-month follow-up, there was an improvement in Mini-Mental scores in non-depressed patients, while depressed patients showed either no change or a slight decline.

A limitation in this study is that the population of stroke patients was primarily lower socio-economic class, black, and male, and patients with severe comprehension deficits were excluded. It is therefore uncertain if the results of this study are applicable to a more general population of stroke patients. In addition, nine of the patients did not have a lesion on CT scan, but these measurements were done during the acute post-stroke period, when the image of the lesion may not have stabilised. The measure of intellectual function was a relatively brief examination, which provided a global measure of cognitive impairment. Although we are now using a more extensive neuropsychological battery, we do not know if the observed cognitive dysfunction was restricted to specific tasks, or represented a more global cognitive decline.

The most significant finding from this study is that depression in stroke patients appears to be associated with their intellectual dysfunction, and that patients with depression and cognitive impairment had smaller lesions than cognitively impaired patients without depression. Although the present data do not prove that depression and cognitive dysfunction are causally connected, this kind of interaction is analogous to that reported in patients with functional depression (Caine, 1981; Kiloh, 1961; McHugh & Folstein, 1979; Nott & Fleminger, 1975; Wells, 1979), and we believe it is another example of 'pseudo-dementia' or dementia of depression. We have also described other similarities between functional and post-stroke depressions, including clinical symptoms, time-courses, and response to dexamethasone suppression test (Robinson *et al*, 1983a; Robinson *et al*, 1984a,c; Lipsey *et al*, 1985). It should be noted, however, that the depression scores in post-stroke patients were somewhat lower than would be expected in functional depressive disorder (Table I). Whether this is the result of changes in scoring which were necessary in a physically impaired population (e.g. on the Hamilton Scale the question of whether the patient stopped working because of their present illness is only answered affirmatively if there was *no* physical impairment which may have contributed to stopping work), or whether the phenomenology of functional and post-stroke depressions are different (e.g. delusional self-blame is very rarely seen in post-stroke patients) is uncertain. Studies are needed of phenomenological comparisons of both the depressive symptoms and specific neuropsychological deficits between these disorders.

If we hypothesise that post-stroke depression and cognitive impairment are causally connected, perhaps by sharing the same underlying mechanism, how might the findings in the present study be construed? McHugh & Folstein (1979) have suggested that a possible mechanism for the dementia of depression is related to alterations in biogenic amine-containing pathways. In the rat, our work, as well as others, has demonstrated that focal brain injury will produce depletions of norepinephrine, dopamine, and/or serotonin concentrations in both cortical and subcortical brain regions (Finkelstein *et al*, 1983; Robinson *et al*, 1975; Robinson, 1979; Robinson *et al*, 1980; Zervas *et al*, 1974). Perhaps a focal ischaemic lesion of the left frontal brain region in humans might lead to depletions of biogenic amine neurotransmitters, producing both depression (Robinson *et al*, 1975; Robinson, 1979; Robinson & Szetela, 1981; Robinson *et al*, 1984a) and loss of concentration or attention, with resultant cognitive decline.

Regardless of the aetiology of intellectual impairments associated with post-stroke depression, these findings have implications for the assessment of stroke patients: if both the lesion itself and depression might lead to intellectual impairment, it would be important to assess the level of depression. In this study, patients with intellectual impairment and depression did not recover over a six-month follow-up period, while patients without depression showed some improvement of intellectual function. We have previously demonstrated in a double-blind treatment study that nortriptyline is effective in the treatment of post-stroke depressions (Lipsey *et al*, 1984). In fact, several patients who received nortriptyline showed some improvement in cognitive function during the six weeks of treatment, and one patient in this study whose depression spontaneously remitted showed some cognitive improvement. Thus, treatment of post-stroke depressions may have a significant impact on both the depression and the course of cognitive recovery in particular, and on the rehabilitiation of stroke patients in general. A study is indicated of the response of these intellectual impairments, associated with depression, to treatment with anti-depressants.

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*Robert G. Robinson, MD, *Professor, Departments of Psychiatry and Neuroscience, Johns Hopkins University School of Medicine, Baltimore, Maryland 21205; Assistant Professor, Department of Psychiatry, University of Maryland School of Medicine, Baltimore, Maryland 21201, USA.*

Karen Bolla-Wilson, PhD, *Post-doctoral Fellow, Department of Psychiatry and Behavioral Science, Johns Hopkins University School of Medicine.*

Edith Kaplan, PhD, *Staff Neurospsychologist, Associate Professor, Psychology Service, VAMC and Department of Neurology, Boston University School of Medicine, Boston, Massachusetts 02130, USA.*

John R. Lipsey, MD, *Assistant Professor, Department of Psychiatry and Behavioral Science, Johns Hopkins University School of Medicine.*

Thomas R. Price, MD, *Professor, Department of Neurology, University of Maryland School of Medicine.*

*Correspondence

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The Validation of the GHQ-28 and the use of the MMSE in Neurological In-Patients

KEITH W. BRIDGES and DAVID P. GOLDBERG

The routine use of screening instruments for psychiatric and cognitive impairment in hospital in-patients has been recommended in the United States. The validity of the scaled version of the General Health Questionnaire (GHQ-28) and the clinical utility of the Mini-Mental State Examination (MMSE) were therefore evaluated in a consecutive series of neurological in-patients (N = 102). Using Receiver Operating Characteristic (ROC) analysis, the discriminating power of the GHQ was very good, and best when using a threshold score of 11/12. The patient sample turned out not to contain any with generalised cortical damage, which casts some doubt on whether the MMSE should be used routinely in all neurological in-patients units in the UK.

This paper assesses the validity of the scaled version of the General Health Questionnaire (GHQ) (Goldberg & Hillier, 1979), by applying Receiver Operating Characteristic (ROC) Analysis (McNeil *et al*, 1975; Metz, 1978), and assesses the clinical usefulness of the Mini-Mental State Examination (MMSE) (Folstein *et al*, 1975) among neurological in-patients.

The GHQ was designed to assist doctors in identifying patients who are likely to have a psychiatric illness. While other versions of this questionnaire have been validated in a number of different medical settings (Goldberg, 1978), reports on the validity of the GHQ-28 have been limited to a community study of randomly selected adolescents (Banks, 1983), and to hospital out-patients with multiple sclerosis (Rabins & Brooks, 1981). The ROC analysis used in this paper was originally developed for use with radar to separate observed variability from innate detectability of a signal. It has since been used in various psychological studies (Swets, 1973) and in some branches of medicine, e.g. in the assessment of diagnostic skills and techniques (Swets *et al*, 1979; Berwick & Thibodeau, 1983; McNeil & Adelstein, 1976). Erdreich & Lee (1981) reported that it is particularly useful in epidemiological studies because it can be used to assess the ability of a screening instrument to detect patients with an illness, while simultaneously excluding patients without an illness, and two studies in psychiatry have employed this technique (Mari & Williams, 1984; Simpson, 1984). The relative discriminating powers of different but competing screening instruments can also be evaluated, using this method.

The MMSE was originally developed as a screening instrument of cognitive impairment among a psychiatric population (Folstein *et al*, 1975), and since its conception, has been used in a number of different clinical settings in the United States (Knights & Folstein, 1977; DePaulo & Folstein, 1978; Cavanaugh, 1983). Like the GHQ, it is not intended to provide a diagnosis of organic disorders, but to help identify patients who require further assessment and investigation. It is reported to correlate with the Weschler Adult Intelligence Scale and Weschler Memory Quotient (Folstein *et al*, 1975; DePaulo *et al*, 1980; Dick *et al*, 1984). Anthony *et al* (1982) and Dick *et al* (1984), in assessing its validity, reported that its optimal sensitivity and specificity are achieved using a threshold score of 23/24. However, they also drew attention to its limitations in assessing visuo-spatial and language functions, as well as in patients over the age of 60, or of poor educational background.

The MMSE has advantages over other standardised assessments of cognitive function. It only takes five to ten minutes to complete, compared to over an hour for the WAIS, and is easy for a clinician to administer at the bedside. It has therefore been recommended for routine bedside assessment of the cognitive state by DePaulo *et al* (1980) and Cavanaugh (1983). Few studies, however, have reported on its use on neurological wards in the UK, and it was therefore thought important to evaluate its clinical utility in this clinical setting.

Method

This study took place in the busy neurology department of a large teaching hospital. During a six-week period, there were 121 consecutive adult admissions to beds situated on three general medical wards. Of these, 19 were either physically too ill to participate, or had very short admissions, leaving 102 patients taking part in the study.

The GHQ-28

Procedure

Two patients had a known dementia with prominent features of frontal lobe dysfunction, and were unable to complete the GHQ in any reliable way. The remaining 100 patients completed the questionnaire on the day of their admission. Within two days, a sub-sample ($n=70$) were psychiatrically assessed in an interview room, using the Clinical Interview Schedule (CIS) (Goldberg *et al*, 1970). A stratified sampling procedure was used, since it was not practicable to administer the CIS to all the patients. The intention was to interview as many as possible of those with a score of 5 or above, and a one-in-four sample of those with scores of 4 or below.

Criteria used to define a psychiatric 'case'

Patients who fulfilled at least two of the following three criteria were regarded as psychiatric 'cases' (Cooper, 1979):

(a) weighted total symptom score of 20 or more, derived from the CIS.

(b) An overall severity score of 2 or more on a five-point scale representing functional impairment: 0 = no psychiatric abnormality, 1 = mild personality deviance, or isolated symptoms, 2 = mild psychiatric disorder, 3 = moderate psychiatric disorder, 4 = severe psychiatric disorder.

(c) A psychiatric diagnosis according to the Mental Disorders Section of the International Classification of Diseases, Injuries and Causes of death (ICD-9).

ROC analysis

This technique is described in detail elsewhere (McNeill *et al*, 1975; Metz, 1978; Hanley & McNeil, 1982; Erdreich & Lee, 1981), but is briefly outlined here. For every possible threshold score of the GHQ-28 (0/1–27/28), a 2×2 contingency table of GHQ responses (Low/High) versus psychiatric caseness (Normals/Cases) is drawn up. From this, the true positive rate (sensitivity) and the false positive rate (1—specificity) are calculated. By plotting the true positive against the false positive rate for each threshold score, a graph is then constructed, which summarises the discriminating performance of the screening instrument across the total spectrum of morbidity. If this discriminating power was not better than chance, a straight line on the principal diagonal would be produced, with an area underneath it of 0.5. A concave curve above this the ROC curve indicates discrimination. An ideal screening instrument would produce a curve indicating 100% true positives before admitting to a single false positive, with an area underneath it of 1.0. In practice, an ROC curve is always intermediate between this and the principal diagonal. It allows a clinician to select the threshold score that is most suitable for his purpose. This will depend on the relative costs and benefits associated with classifying a patient with an illness as normal and classifying a normal person as ill (McNeil *et al*, 1975), and thus includes consideration of the trade-off between sensitivity and specificity.

The MMSE

The MMSE was administered to 101 patients on the day of their admission. One patient could not tolerate the test—a 25 year-old male, with an advanced juvenile Huntington's chorea. A score below 24 was taken to indicate probable cognitive impairment.

TABLE I
Demographic characteristics

Age range yrs	*16–24*	*25–34*	*35–44*	*45–65*	*65+*	*mean SD*
males $n=57$	7	10	4	26	10	47.8±17.8
females $n=45$	3	14	13	10	5	41.5±22.9

Social class	*I*	*II*	*III N–M*	*III M*	*IV*	*V*	*not known*
males $n=57$	2	14	5	22	3	9	2
females* $n=45$	4	15	8	14	3	1	0

Marital status	*Single*	*Married*	*Divorced/separated*	*Widowed*
males $n=57$	16	33	4	4
females $n=45$	5	33	5	2

*Based on husband's employment, or on their father's if living at home or on their own if neither of these applied.

TABLE II

Data showing correction for stratified sampling procedure using a threshold score of 11/12

	Total number of respondents	*Subsample assessed by CIS*			*Weighted data*	
		Total number	*Non-cases*	*Cases*	*Non-cases*	*Cases*
GHQ Score range						
12–28	43	40	11	29	11.8	31.2
5–11	22	20	13	7	14.3	7.7
0–4	35	10	10	0	35	0
Totals	100	70	34	36	61.1	38.9

TABLE III

Sensitivity and specificity for different GHQ-28 threshold scores

Threshold score	*Sensitivity*	*Specificity*
3/4	100	51.1
4/5	100	57.4
5/6	97.4	59
6/7	96.7	61.6
7/8	96.9	66.7
8/9	91.5	69.9
9/10	85.3	73.9
10/11	85.3	73.9
11/12	80.2	80.7
12/13	76.4	82.9
13/14	58.1	91.2
14/15	50.4	94.6
15/16	34.7	94.4
16/17	27.4	98.0
17/18	20.2	98.2
18/19	14.8	98
19/20	12.3	98
20/21	12.7	100

Other clinical information

The medical notes, results of investigations, and discharge letters of each patient were all examined at a later date for any evidence of organic psychosyndrome found by the neurologists, as well as for the diagnosis of the patient's physical disorder. Investigations included computed tomography, carotid angiography, myelography, electrophysiological studies, relevant haematological, biochemical, bacteriological, and viral tests, and detailed psychometric testing by clinical psychologists, ordered by the neurologists.

Results

Patient characteristics

(a) *Demographic (Table I)*

In general, the sample was reasonably representative of the general population of the city in which the hospital is situated in terms of age. However, a greater proportion were married, and female patients were over-representative of higher social classes and under-representative of lower social classes ($X^2 = 17.59$; df = 5; $P = 0.01$) (OPCS, 1971 & 1981).

(b) *Diagnostic Categories of Physical Disorders*

According to the neurologist from information in medical notes and discharge letters 70 had a definite organic disorder, while in 26 the physical diagnosis was uncertain; three patients had a 'functional' disorder, while one proved not to be ill.

Validation of the GHQ-28

Using the stratified sampling procedure, 28.5% of patients with GHQ scores 0–4, and 92.3% of those with scores 5–28 were assessed, using the CIS. The number of 'cases' and 'non-cases' were then proportionally increased so that they applied to the total number of patients completing the GHQ (Goldberg, 1978). This weighting procedure was repeated in a stratified manner for all possible threshold scores as illustrated by using a threshold score of 11/12 (Table II). Using weighted data, 2 × 3 contingency tables for each threshold scores were drawn up; from this, the validity coefficients were calculated (Table III), and the ROC curve plotted (Figure 1). The area under this curve, as measured by a planimeter, was 0.88. This analysis showed that the best trade-off between sensitivity and specificity was achieved using a threshold score of 11/12. Based on this threshold, and after corrections for the sampling procedure, the validity coefficients were also determined for each sex (Table IV).

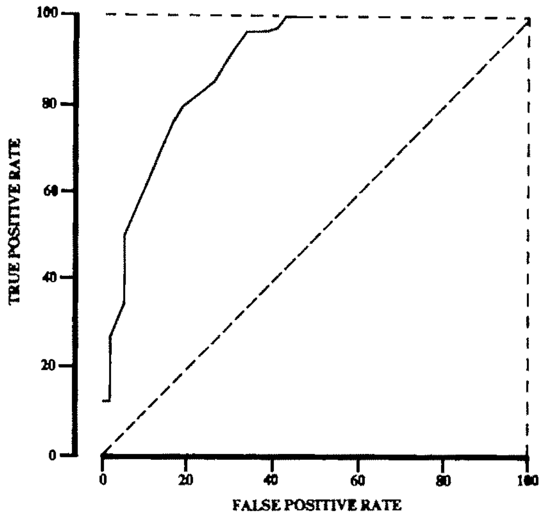

FIG. 1 Receiver operating characteristic curve of the GHQ-28.

TABLE IV
Summary of validity coefficients using GHQ threshold score 11/12

Validity coefficient	*Combined sexes*	*Male*	*Female*
Sensitivity	80.2%	78.4%	81.2%
Specificity	80.7%	85.3%	70.9%
Positive predictive value	72.6%	66.7%	76.0%
Misclassification	19.5%	16.6%	23.6%
Estimated prevalence of psychiatric morbidity	38.9%	27.4%	53.2%

Usefulness of the MMSE

Of the 101 patients who were assessed by the MMSE, the neurologists found evidence of an organic brain syndrome only in two patients. Both had prominent features of frontal lobe dysfunction a 52 year-old female who was thought to have Pick's Disease, and a 75 year-old male with a Steele-Richardson syndrome; both, however, had MMSE scores in the normal range (⩾24). Three other patients with no evidence of a dementia scored below 24: a 65 year-old man with Parkinson's disease and severe depressive illness, a 25 year-old man with a marked personality disorder and alcohol dependence (who was not fully cooperative during the test), and a 77 year-old woman with a post-herpetic neuralgia who admitted to poor concentration due to severe head pains. All patients otherwise scored within the normal range.

Discussion

This study has shown that the GHQ-28 is a valid and useful screening instrument of psychiatric morbidity in neurological in-patients. The results of the ROC analysis demonstrate that it is good at discriminating between patients with, and those without a psychiatric illness.

This study has also shown that the best results with the GHQ-28 are obtained with a very much higher threshold score than that recommended in the test manual (Goldberg, 1978). This seems to be due to the severe neurological illnesses in this particular patient population, which caused many non-cases to report symptoms on the somatic and social dysfunction sub-scales. A subsequent item analysis (Bridges, 1983), showed that 27 out of the 28 items still had a discriminating power, so that nothing could be gained by shortening the questionnaire. The need for a higher threshold score is in keeping with the observations of other studies which have found that patients with physical symptoms tend to score high on the GHQ (Goldberg, 1978; Maguire *et al*, 1974; Finlay-Jones & Murphy, 1979; Rabins & Brooks, 1981). It also supports the suggestion of Kirk & Saunders (1979) in their assessment of the use of the GHQ-60 in neurological out-patients that a more accurate estimate of the prevalence of psychiatric morbidity in these subjects could only be achieved using a higher threshold score than originally recommended. However, their study was limited by their understandardised case-finding procedure, and because they regarded any probable psychiatric disturbance as a false positive if it presented as an organic disorder. In our study. although the higher threshold score resulted in a reduction in the sensitivity of the GHQ, it did improve its specificity and positive predictive value.

The specificity and sensitivity, using the higher threshold score, are lower than those reported by Banks (1983) among randomly selected adolescents (sensitivity 100%, specificity 84.5%, using a cutting score of 5/6) and by Rabins & Brooks (1981) assessing neurological out-patients (both coefficients being 92% with a cutting score of 4/5). This difference may have been because both of these other studies used the PSE (Wing *et al*, 1967) as their method of case-identification. Nevertheless, the validity coefficients determined in our study, are comparable with those reported for other versions of the GHQ (Goldberg, 1978, 1983). It is noteworthy that although female patients had a higher misclassification rate, the positive predictive value of the instrument for them was better than in males; this would be in keeping with the observations that females tend to report symptoms more than men (Goldberg, 1972, 1978).

Although generally higher, the estimated prevalence of psychiatric morbidity (excluding dementia) in this sample of neurological in-patients is comparable to the findings of others surveys on medical in-patients which used a standardised psychiatric assessment linked to specific operational criteria, and supports the observations made in the United States by DePaulo & Folstein (1978) and DePaulo *et al* (1980) that a substantial level of psychiatric morbidity exists in patients cared for by neurologists. The extent to which this morbidity was detected by the neurologists was very small, and the chance of its detection was found to be greater for male patients (Bridges & Goldberg, 1984).

It was not possible to make a full evaluation of the usefulness of the MMSE, since our case material turned out not to contain any patients with generalised cortical damage who should have been detected by the instrument, so that we cannot make any estimate of sensitivity. However, if the two cases with frontal cortical lesions are excluded from consideration, then the remaining 99 patients can be divided into 96 true negatives and three false positives, giving a specificity of 97%.

The prevalence of organic disorders which are likely to give rise to cognitive impairment in our patient sample contrasts markedly with the American studies, which reported that between 28 and 32% of patients had MMSE scores indicative of cognitive impairment (Knights & Folstein, 1977; DePaulo *et al,* 1980; Cavanaugh, 1983). Dick *et al* (1984) also reported a much higher proportion of consecutive patients who were judged to be cognitively impaired, but they also included patients from neurosurgical wards. It would appear from this that the prevalence of different organic disorders causing cognitive impairment which are treated by neurologists varies from one hospital unit to another. If this is the case, it suggests that if the MMSE is used routinely, as recommended by DePaulo *et al* (1980) and Cavanaugh (1983), it is likely to be of value only in patient populations in which the prevalence of cognitive impairment is relatively high.

Finally, although screening instruments have undoubted epidemiological value, it would be wrong for clinicians to use them as substitutes for, rather than as aids to their own assessment of their patients. The assessments of such morbidity should be as much a part of history-taking and examination as is the assessment of other systems which may not be overtly or directly associated with the patient's presenting complaints.

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*K. W. Bridges, MSc, MRCPsych *Consultant Psychiatrist, Department of Psychiatry, Manchester Royal Infirmary, Oxford Road, Manchester M13 9WL (formerly Clinical Research Fellow, University of Manchester).*

D. P. Goldberg, DM, FRCP, *Professor, Department of Psychiatry, University Hospital of South Manchester, West Didsbury, Manchester M20 8LR.*

*Correspondence

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Depression, Hopelessness and Suicide in Chronic Schizophrenia

ROBERT E. DRAKE and PAUL G. COTTON

Hospital records for 104 schizophrenic patients, 15 of whom subsequently committed suicide, were rated blindly for individual depressive symptoms comprising DSM III major depressive episode, and for hopelessness. Our results indicate that a large proportion of schizophrenic patients experienced major depressive episodes, and that these can be reliably identified. Presuicidal schizophrenics also experienced depressed mood, but only a minority developed the full syndrome; they typically exhibited the psychological, but not somatic symptoms. The relationship between depression and suicide disappears when hopelessness is taken into account.

Schizophrenia carries an increased risk of both depression and suicide. Siris *et al* (1981) found that during hospital admissions, 40% of a cohort of schizophrenics expressed subjective sadness, 22% met Research Diagnostic Criteria (RDC) (Spitzer *et al*, 1978) for minor depressive episode, and 6% met RDC criteria for major depressive episode. Mandel *et al* (1982) found that 22.3% of schizophrenics who were followed for one year after index admission developed depression according to the Hamilton Depression Scale (Hamilton, 1967), based on a score of at least 16. Evenson *et al* (1982) found that the age-adjusted suicide rate for schizophrenics was nearly ten times that of the full population, while Miles (1977) reviewed 34 studies of suicide among schizophrenics and estimated that 10% kill themselves.

The appearance of depression in schizophrenia is perhaps the most frequently identified suicide risk factor (Achte *et al*, 1966; Beisser & Blanchette, 1961; Niskanen *et al*, 1974; Sletten *et al*, 1972). In separate controlled studies, Cohen *et al* (1964) and Roy (1982) found that schizophrenics who kill themselves are more likely to have experienced depression than schizophrenic controls. However, the precise nature of the relationship between depression and suicide in schizophrenia remains unclear (Drake *et al*, 1985). With the exception of Roy's study, in which depression was defined according to the DSM III criteria for major depressive episode, standardised definitions of depression have not been used. Since many schizophrenics develop depressive symptoms, and various authors have emphasised different aspects of depression, the critical parameters for identifying high suicide risk await clarification.

Hopelessness is one distinct aspect of the depressive syndrome that has been associated with suicidal thoughts and behaviour (Virkkunen, 1976; Yarden, 1974). It can be defined objectively as a set of negative expectancies about the future (Stotland, 1967). Beck's analysis (1967) of the individual items on his Depression Inventory showed that suicidal wishes correlated more highly with hopelessness than with any other item. A depressed patient may exhibit sadness, feelings of worthlessness, and somatic complaints, yet continue to hold hope for the future and not be suicidal; however, when hopelessness develops, suicidal intent tends to appear also. Hopelessness and suicidal intent have been strongly linked in several studies of subjects attempting suicide and with suicidal ideas (Beck *et al*, 1975; Kazdin *et al*, 1983; Minkoff *et al*, 1973; Wetzel *et al*, 1980), but we know of no comparable study of completed suicides.

The present study examines the individual clinical features of depression, including hopelessness, and their relationship to major depressive episodes and subsequent suicides in a group of chronic schizophrenic inpatients. Although our previous report (Drake *et al*, 1984) suggested the importance of hopelessness, our method did not allow a careful dissection of depressive symptoms. The purposes of this study were to determine which depressive features are associated with completed suicide in schizophrenia and to clarify the role of hopelessness in schizophrenia.

Method

Subjects

The sample consisted of 15 inpatients with schizophrenia who subsequently committed suicide, and 89 similar patients who did not commit suicide, during a 3- to 7-year follow-up. All subjects were admitted to hospital in an urban mental health system between 1976 and 1980, and met DSM III criteria for schizophrenia according to blind review of case records by two psychiatrists. All known suicides among cases of schizophrenia during this interval were included in the sample, and their last admissions before their suicide served as the index admission for ratings. Suicides were validated by clinical review and death records. Controls were identified through consecutive admissions, and these admissions served as the index events for rating. Patients who were aged over 65 years, were long-stay patients in hospital (more than two years), were admitted very briefly (less than two weeks), or were lost to follow-up, were excluded. Details of the sample are described elsewhere (Drake *et al*, 1984).

Rating depressive symptoms

As our previous data collection did not permit an analysis of depressive symptoms over a period of time, we abstracted records from the index hospital admission for this study to include all daily progress notes regarding patients' concerns and symptoms, and to exclude any reference to subsequent suicidal behaviour. Two research assistants, blind to outcome, independently rated the records for features of depression according to DSM III criteria. In addition, they rated hopelessness according to statements similar to those in the Hopelessness Scale designed by Beck *et al* (1974). Thus, hopelessness was considered present only when the patient made explicit comments expressing a negative outlook toward the future. For example, one hopeless patient stated that he knew he would never be able to work again. Because the severity of depressive symptoms was difficult to evaluate from the case records, all judgements were dichotomous, viz.—present versus absent. Depressive symptoms were rated as present only when they coincided temporarily with a period of depressed mood, so that a symptom such as 'diminished thinking capacity' which coincided with a period of psychotic decompensation was rated absent as a depressive symptom.

Results

As described elsewhere (Drake *et al*, 1984), the suicides and controls were similar in terms of demographic features and psychiatric histories (Table I). Both groups were young, but manifested severe, chronic illness and poor psychosocial functioning. A large proportion had made previous suicide attempts.

Depression ratings

A majority of patients (54%) demonstrated 'depressed mood' which persisted for at least 2 weeks, and most of the other depressive symptoms occurred frequently (Table II). 'Loss of interest or pleasure' and 'diminished thinking or concentration' were exceptions because, when present, they were not usually associated temporally with depressed mood. In all, 21% of the sample met DSM III criteria for major depressive episode. These figures do not represent incidence data, since the sample was preselected for youth, non-institutionalisation, lengthier hospital admissions, and chronicity. However, the data do reflect the large amount of depression in cases of schizophrenia at risk for suicide.

Inter-assessor reliability on individual depressive items was determined according to coefficient kappa (Bartko & Carpenter, 1976) on the basis of ratings by two independent raters of 30 randomly selected records. These figures (Table II) also reveal that items were rated reliably, with the exceptions of the two low-incidence variables, for which kappa scores could not be determined, and 'psychomotor disturbance', which can be associated with psychosis, agitation, or side-effects of medication as well as depression.

Table III shows a correlation matrix for the depressive symptoms and major depressive episode. These variables represent the depressive symptoms comprising major depressive episode from DSM III. Except for the few relationships so indicated, all correlations showed significant phi coefficients; the variables were strongly intercorrelated and related to a diagnosis of major depressive

TABLE I
Characteristics of suicides and controls

	Suicides (n=15)	*Non-suicides (n=89)*	*Significance level (p value)*
Mean age at hospital admission (years)	31.7	31.3	NS
Sex (% male)	60%	54%	NS
Marital status (% unmarried)	100%	93%	NS
Employment (% unemployed)	93%	93%	NS
Duration of illness (years)	8.4	7.2	NS
Mean number of hospital admissions	7.8	6.5	NS
Previous suicide attempt	73%	49%	NS
DSM III chronic schizophrenia	93%	92%	NS
DSM III subchronic schizophrenia	7%	8%	NS

Significance levels refer to t tests or chi-square tests.

TABLE II
Depressive symptoms in total sample

	Total sample (n=104)		*Reliability (kappa coefficient)*
	n	*%*	
Depressed mood	56	54%	0.55
Appetite or weight disturbance	21	20%	0.84
Sleep disturbance	31	30%	0.65
Psychomotor disturbance	55	53%	0.10
Loss of interest or pleasure	7	7%	—*
Loss of energy	10	10%	0.43
Worthlessness, self-reproach, or guilt	33	32%	0.77
Diminished thinking or concentration	6	6%	—*
Suicidal ideas	50	48%	0.74
Major depressive episode	22	21%	1.0
Hopelessness	28	27%	0.83

*Kappa scores could not be determined because of lack of variance.

TABLE III
Intercorrelations among factors

Factor number and name	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*
1 Depressed mood	0.31	0.40	0.25	0.23	0.24	0.54	0.23	0.70	0.47
2 Appetite or weight disturbance		0.48	0.11*	0.09*	0.09*	0.25	0.19	0.27	0.54
3 Sleep disturbance			0.32	0.29	0.36	0.38	0.29	0.39	0.67
4 Psychomotor disturbance				0.23	0.31	0.29	0.15*	0.23	0.33
5 Loss of interest or pleasure					0.48	0.28	0.12*	0.26	0.49
6 Loss of energy						0.21	0.34	0.15*	0.49
7 Worthlessness, self-reproach, guilt							0.19	0.49	0.60
8 Diminished thinking or concentration								0.10*	0.39
9 Suicidal ideas									0.48
10 Major depressive episode									

*Phi coefficients not significant at $P = 0.05$. All others significant at $P < 0.05$.

episode. Taken together, the matrix of correlations supported the internal consistency of the secondary diagnosis of major depressive episode in chronic schizophrenia.

Depression and suicide

A comparison of suicides and controls (Table IV) shows that suicides were much more likely to manifest persistent depressed mood as well as many of the other features of depression during index hospital admission. They were not, however, significantly more likely to meet the criteria for major depressive episode. Breaking down the depressive symptoms into somatic and psychological symptoms reveals why: the suicides clearly demonstrated the psychological features of depression, including hopelessness. Of the somatic symptoms, only psychomotor disturbance, which was frequent in the entire sample and not rated as reliably as other variables, was characteristic of the suicides.

Table V illustrates the relative contributions of depression and hopelessness to suicide. Although the presence of persistent depressed mood increased the probability of suicide, severity of depression, as measured by major depressive episode, did not further increase the risk of suicide. On the other hand, the development of hopelessness in addition to depressed mood significantly augmented the probability of suicide. Furthermore, in the absence of the hopelessness, depressed schizophrenics were at no greater statistical risk for suicide than non-depressed schizophrenics.

TABLE IV
Depressive symptoms and suicide

Variable	*Suicides* (*n*=*15*)	*Non-suicides* (*n*=*89*)	*Significance*[1]
Severity of depression			
Persistent depressed mood (at least 2 weeks)	80%	48%	$P<0.01$
Major depressive episode (DSM III)	33%	19%	NS
Somatic Symptoms			
Appetite or weight disturbance	20%	24%	NS
Sleep disturbance	40%	31%	NS
Psychomotor disturbance	80%	51%	$P<0.05$
Loss of energy	20%	8%	NS
Psychological symptoms[2]			
Worthlessness, self-reproach, or guilt	53%	23%	$P<0.01$
Suicide ideas	87%	44%	$P<0.01$
Hopelessness	67%	20%	$P<0.01$

[1] Significance levels refer to chi-squared tests.
[2] Loss of interest or pleasure and diminished thinking or concentration are omitted from this table because of low incidence.

TABLE V
Depression, hopelessness and probability of suicide

	Total *n*	*Suicide* *n*	*Probability of suicide*
Entire sample	104	15	0.14
Patients with depressed mood	56	12	0.22
with major depressive episode	22	5	0.23
with hopelessness	27	10	0.37
without hopelessness	29	2	0.07
Patients without depressed mood	48	3	0.06

Discussion

This study supports the argument of Beck *et al* (1975) that the association between depression and suicide is due to their common link with hopelessness. Since patients rarely become hopeless in the absence of depressed mood, hopelessness may operate as a powerful potentiating variable, so that depression becomes a clinically meaningful predictor of suicide only when hopelessness develops. Our findings also suggest that other psychological features of depression, such as feelings of worthlessness and suicidal ideas, are important harbingers of suicidal behaviour.

It is possible that presuicidal patients appear depressed and hopeless while in hospital, and then develop the full depressive syndrome in the community, before committing suicide; however, this occurrence did not account for our results. Follow-up interviews with therapists who treated these patients just before their deaths (Cotton *et al*, 1985) revealed that most continued to develop progressive hopelessness about their lives following index hospital admission, but did not manifest the somatic symptoms of depression.

A more likely explanation of our results is that these patients appeared depressed because they despaired about their future lives with chronic mental illness. These suicide victims had shown high premorbid achievement, high self-expectations of performance, and high awareness of pathology (Drake *et al*, 1984). For example, 73%, compared with 29% of the non-suicides, were college-educated. Given their inability to achieve major life goals, they felt inadequate, feared further deterioration of their mental abilities, and decided to end their lives rather than continue living with chronic mental illness. To the extent that their decisions represented realistic estimations of current and future functioning in relation to goals, rather than mood-distorted perceptions of the future, perhaps these patients should be considered to suffer from despair rather than depression.

One limitation of this study is the use of case record data. Data were gathered prospectively and rated blindly and for the most part reliably, but the original collecting and handling of information from unstructured interviews by different clinicians raise questions of random error. To the extent that such error was introduced by these procedures, statistical relationships and clinical meaningfulness of the results should be diminished. However, the coherence and strong statistical relationships in our results suggest that they are in fact based on accurate information.

Our finding that 'diminished thinking or concentration' and 'loss of interest or pleasure' were not usually associated with depressive symptoms may explain the differences between our results and those of Roy (1982), who found that major depressive episodes preceded suicides. Since he did not publish ratings of individual symptoms or reliability data, comparison between the two studies is difficult. However, our ratings of major depressive episodes were made with high reliability, and it seems unlikely that random error could account for the modest relationship between major depressive episode and suicide.

Our inability to rate psychomotor disturbance reliably was a more complicated issue, particularly since this variable was modestly related to suicide. Psychomotor agitation or retardation can be related to depression, but also to a variety of other problems, viz. psychosis, anxiety, or side-effects of medication; psychomotor changes could therefore be related to suicide as a function of any or all of these factors. One possible explanation is the association between akathisia and suicidal behaviour (Drake & Ehrlich, 1985; Shear *et al*, 1983).

Despite these problems, this study had several advantages over previous research. Firstly, it used a high-risk comparison group of young, non-institutionalised cases of DSM III schizophrenia, and thereby replicated the clinical situation; these are the patients about whom important clinical decisions must be made. Secondly, it deals with completed suicides rather than those attempting suicide or with suicidal ideas; it therefore provided an important extension of previous findings. Thirdly, it was the first study of depression and suicide associated with schizophrenia to examine well-defined aspects, rather than a more global measure of depression. Finally, all ratings were made blindly, with tests of reliability.

It was concluded that a high proportion of patients admitted to hospital with schizophrenia exhibit depressive symptoms; these patients often manifest the full depressive syndrome, defined by major depressive episode in DSM III. Before they commit suicide, cases of schizophrenia also frequently appear depressed, but only a minority experience major depressive episodes. Instead, they are likely to experience hopelessness defined as negative expectancies about the future and other psychological features of depression. Neither somatic symptoms nor depressed mood alone indicate a high risk of suicide in schizophrenics. In the absence of hopelessness, depressed cases of schizophrenia are at no greater risk for suicide than non-depressed patients with schizophrenia.

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*Robert E. Drake, MD, PhD, *Assistant Professor, Medical Director, Community Mental Health Services, Dartmouth Medical School, Hanover, New Hampshire, USA.*

Paul G. Cotton, MD, *Assistant Professor, Harvard Medical School, Medical Director, Pembroke Hospital, Pembroke, Massachusetts, USA.*

*Correspondence

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Pharmacokinetics and Therapeutic Efficacy of Haloperidol Decanoate after Loading Dose Administration

H. De CUYPER, J. BOLLEN, H. M. van PRAAG and D. VERSTRAETEN

For this open study, we selected 21 chronic psychotic female in-patients (16 of them schizophrenics) who were being maintained on oral neuroleptics. After a wash-out period, they were treated by intramuscular depot injections of haloperidol decanoate, once a month for four months. The dose was calculated from the previous oral dosage, and the amount of the first injection was double that of the three following injections. Relatively stable plasma levels of haloperidol were achieved with the first injection, and corresponded to those observed with oral medication. A very significant correlation was found between plasma level and the dose administered, but not between plasma level and therapeutic effect. The clinical condition of about two-thirds of the patients remained unchanged or improved, compared with the period of oral treatment. During the first two months of treatment, there was more rigidity and tremor, but from the third month, the extrapyramidal symptoms were less pronounced than during the period of oral neuroleptics.

The development of depot preparations represents considerable progress in the pharmacotherapy of chronic and recurrent psychoses. The administration of a single dose of a neuroleptic, the activity of which persists for at least one week, sometimes several weeks, practically solves the problem of non-compliance: thus the number of psychotic relapses is reduced and the duration of the hospitalisations shortened (Johnson, 1979). In addition, first-pass metabolism can be avoided by the parenteral administration; this may be an explanation for the better therapeutic response to depot preparations than to orally administered neuroleptics.

Long-acting neuroleptics have been developed from substances with varying chemical structures, such as phenothiazines, thioxanthenes, and diphenylbutylpiperidines. In 1978, a long-acting butyrophenone derivative became available: haloperidol decanoate (Figure 1). When dissolved in sesame oil and injected into muscle, haloperidol decanoate has a long-lasting activity, due to its slow release from the depot sites. The active compound is released

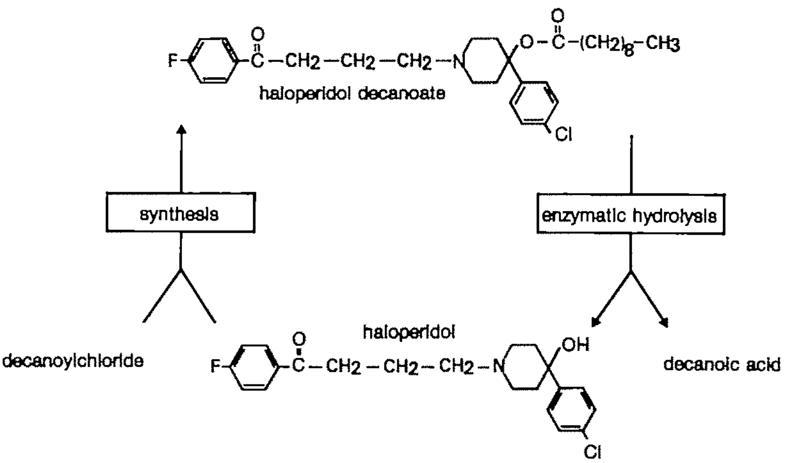

FIG. 1 Chemical structure of haloperidol and its decanoate ester.

after enzymatic hydrolysis by esterases, which are present in the blood and the tissues. In dogs, depending on the dose, a pharmacological effect lasting for more than one month has been obtained (Niemegeers *et al*, 1981).

Five clinical studies—four in open and one in double-blind conditions—have confirmed the therapeutic efficacy and the safety of haloperidol decanoate as a depot preparation (Deberdt *et al*, 1980; Gelders *et al*, 1982; Viukari *et al*, 1982; Youssef, 1982; Zissis *et al*, 1982). Most of the studies used a monthly dose of approximately 20 times the daily oral dose, since the bioavailability of an oral haloperidol dose is usually 60%–70% of the parenteral one (Forsman & Öhman, 1977).

Pharmacokinetic studies have shown that after a single intramuscular injection of haloperidol decanoate, a peak in haloperidol plasma levels is reached between the third and the tenth day (De Buck *et al*, 1981; Heykants & Gelders, 1984). The plasma concentrations then decrease very slowly, with a half-life of three or four weeks, depending on the dose. Steady-state plasma levels of haloperidol are reached between the second and third injection of haloperidol decanoate (Deberdt *et al*, 1980; Parent *et al*, 1981).

As the use of a loading dose can sometimes shorten the time needed to reach steady state, the present pharmacokinetic study aimed at investigating whether the administration of a double dose during the first month, followed by a single dose during the three subsequent months, would result in steady-state plasma levels from the beginning of the treatment.

Method

1. Patient selection

The group under investigation consisted of 21 chronic female in-patients of the Sancta Maria psychiatric clinic in Sint-Truiden. Admission was mostly due to chronic psychotic symptoms such as delusions, hallucinations, decreased affect, and loss of initiative. By DSM III criteria, 16 patients had chronic schizophrenia and five had other diagnoses (paranoid, personality and conduct disorders, or mental retardation). The mean age was 58 years (range 21–67), and the mean duration of hospitalisation was 26 years (range 1.5–41). All the patients selected had already been receiving a maintenance dose of orally administered neuroleptics. In 12 cases, the neuroleptic medication consisted of haloperidol alone (1.5–30 mg). The remaining patients received, as their main neuroleptics, chlorpromazine (25–300 mg), perphenazine (8–24 mg), or thioridazine (150–200 mg). In some cases, these neuroleptics were combined with each other, in some they were associated with a minor tranquilliser or a hypnotic drug. Twelve patients had concomitantly received antiparkinsonian medication, namely orphenadrine (Disipal) or dexetimide (Tremblex), two anticholinergic agents.

2. Study design

This was an open (non-blind) study with a total duration of 21 weeks, including four months of depot haloperidol decanoate administration. After one week of wash-out, the previous oral neuroleptics were replaced by monthly intramuscular injections of haloperidol decanoate, using 1 ml ampoules of 50 or 100 mg. The dose of haloperidol decanoate for each patient was calculated from her previous oral dose, using a table of neuroleptic equivalence (Suy *et al*, 1982), and the patients were divided into three subgroups: low dosage ($n=7$), intermediate dosage ($n=7$), and high dosage ($n=7$).

For their first injection, the patients received a loading dose of haloperidol decanoate (100–400 mg). For the second injection, half of this loading dose was administered, and this maintenance dose was kept constant for three months, unless an adaptation of the dosage became necessary because of disturbing side-effects or lack of therapeutic effectiveness. The twelve patients who had received antiparkinsonian medication concomitantly with previous oral neuroleptics were kept on their antiparkinsonian agent during the period of investigation. The remaining patients received no antiparkinsonian drugs, except when disturbing extrapyramidal symptoms appeared (this occurred in three cases).

3. Evaluation

Therapeutic effect

For the evaluation of therapeutic effect, two scales were used: the Brief Psychiatric Rating Scale (Overall & Gorham, 1962), completed at the end of each week by the treating psychiatrist; and the 30-item Nurses Observation Scale for In-patient Evaluation (Honigfeld *et al*, 1966), completed weekly by the research nursing staff. These will be referred to as the BPRS and NOSIE-30 scales. Patients were rated on these scales during the last four weeks of oral treatment, during the week of wash-out, and during depot treatment (4 × 4 weeks).

Side-effects

Frequency and severity of side-effects (hypokinesia, rigidity, tremor, akathisia, salivation, somnolence, and depression) were scored at the end of each week by the treating psychiatrist. For this purpose, a four-point rating scale was devised by the authors of this article. Side-effects were evaluated over the same 21-week period as therapeutic effects (see above).

Complete blood analyses were performed at the start of the trial, two weeks after the first and second injections, and at the end of the investigation. At the same time, liver function (transaminases), kidney function (urea, creatinine) and blood sugar content were examined.

Plasma drug levels

The plasma levels of haloperidol were determined by radio-immunoassay (Van Den Eeckhout *et al*, 1980).

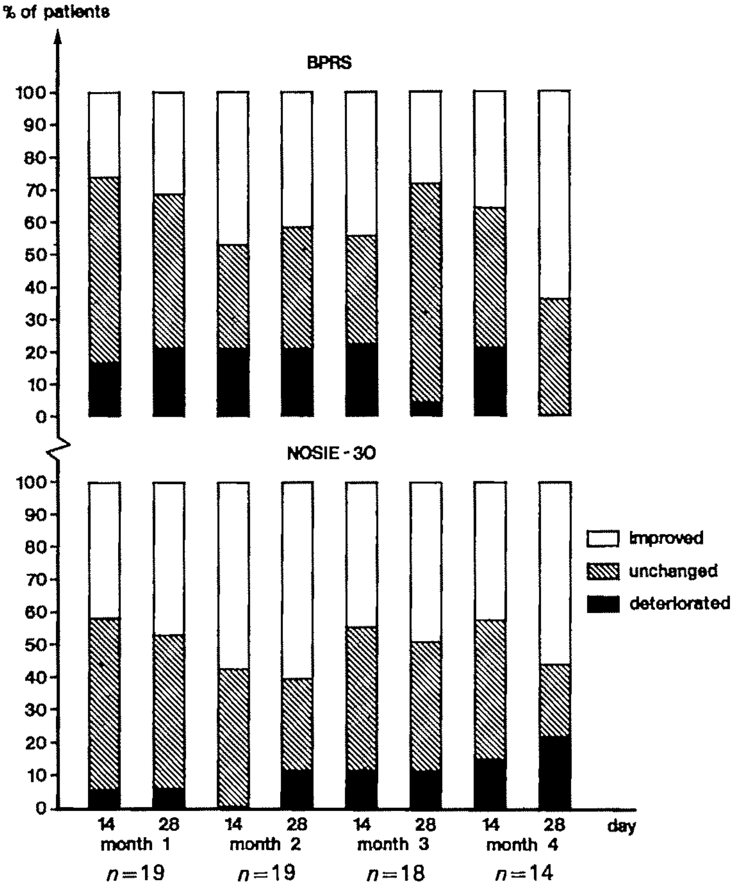

FIG. 2 Variations in group scores on the Brief Psychiatric Rating Scale and the Nurse's Observation Scale for In-Patient Evaluation during the four months of the trial, compared (for each patient) with the mean of four oral-treatment measurements.

Blood samples were taken 3 hours, 8 hours, 24 hours and 48 hours after each injection of haloperidol decanoate and also on the 7th, 14th, 21st and 28th day after each injection. In the 12 patients who previously received haloperidol as their only neuroleptic medication, the plasma level of haloperidol was also assayed in a blood sample taken 14 hours after the last oral intake.

Statistical analysis

The therapeutic effect was evaluated by means of an analysis of variance on the BPRS scores and on the NOSIE-30 scale, according to the Randomised Block Design, with $k=8$, 4 and 4 (Kirk, 1968). Because of drop-out during the course of the investigation, the data were not analysed all together, but in three stages, i.e. months 1+2, month 3, and month 4. For the paired comparisons between observations, contrast analysis with the Bonferroni t-test was performed (Kirk, 1968).

Results

For the evaluation of therapeutic effects, side-effects, and plasma levels, only those patients were included who followed strictly the scheme of the experiment: thus 19 patients were evaluated for months 1+2, 18 for month 3, and 14 for month 4. The reasons for deviation from the original design were: non-intentional change of dosage schedule ($n=1$); discharge ($n=2$); clear day-time somnolence ($n=1$); and an exacerbation of psychotic symptoms ($n=3$). The worsening of psychotic symptoms necessitated small dose changes for the three patients concerned, during months 3 and 4.

1. Therapeutic effect

Total BPRS and NOSIE-30 scores

The changes in the clinical situation, as assessed by the total scores of BPRS and NOSIE-30, are shown in Figure 2. Results on the BPRS were regarded as 'improved' or

TABLE I

Results of analysis of variance for the sum scores of BPRS and NOSIE–30 (mean of weekly total scores) over the three phases of the trial, compared with the means of the oral-treatment values

Month	*n*	*BPRS*		*NOSIE-30*	
		F	*P*	F	*P*
1+2	19	0.69	0.696	5.67	<0.0005
3	18	1.02	0.401	2.05	0.096
4	14	2.71	0.040	4.50	0.003

'deteriorated' according to an *ad hoc* criterion of at least 4 points change in the total score, compared with the mean of the four oral-treatment measurements. Similarly for the total score on the NOSIE-30, we specified a change of at least six points. Figure 2 shows that in the majority of cases, on both scales, the clinical situation was unchanged or improved.

Analysis of variance of total BPRS scores (Table I) detected no significant change during months 1+2 or month 3, but in month 4, the weekly observations showed a significant improvement over the mean of the four oral-treatment scores. The NOSIE-30 scores showed a very significant improvement over oral-treatment scores in the first two months: this change dropped below the 10% level of significance in month 3, before returning to statistical significance ($P<0.05$) in month 4.

Contrast analysis of the BPRS scores (paired *t*-test) showed that at the end of the loading-dose phase (week 4), the therapeutic effect achieved was equal to the one obtained previously with oral neuroleptics: the difference between the scores of week 4 and the oral-treatment mean was not significant. After the dose was reduced by 50%, the clinical condition appeared to remain constant: the contrasts between oral treatment and weeks 8 and 12 respectively were not significant. At the end of the study (week 16), a significant improvement as compared with the oral-treatment condition was observed ($P\leqslant 0.005$).

Contrast analysis of the NOSIE-30 scores showed significant improvement between the oral-treatment mean and weeks 4, 8 and 16 ($P\leqslant 0.003$). The contrast between oral treatment and week 12 was not significant.

Cluster analysis of BPRS and NOSIE-30 scores

Analysis of variance of BPRS clusters (anxiety, anergia, activity, thought content, and hostility) showed a significant overall difference only for the cluster 'hostility' during months 3 and 4 of the trial.

Analysis of variance of NOSIE-30 clusters (social competence, personal neatness, social interest, retardation, irritability, and manifest psychosis) showed a significant overall difference for the clusters 'social competence' and 'irritability' at all stages of the trial. Additionally, the cluster 'retardation' was significantly different from the oral-treatment mean in the fourth month.

2. Side-effects

Table II reviews the frequency and severity of side-effects. Compared with the period of oral neuroleptic treatment, there was an increase in rigidity and tremor during the first two months of the investigation, such that three patients were put on orphenadrine (3 × 50 mg daily). From the third month onwards, hypokinesia, rigidity, tremor, and akathisia were less pronounced than during the period with oral neuroleptics. Daily somnolence appeared to be reduced throughout treatment with the long-acting neuroleptic; nor did the treatment cause depression. In one patient, fibrosis developed at the site of injection, and another patient had an epileptic seizure, though she had no history of epilepsy.

TABLE II

Numbers of patients with various side-effects before the trial (Week −2) and at different times during the depot treatment. The number of patients in whom the side-effect was at least moderately severe is given in brackets

Side-effect	*Oral medication (Week −2)*	*Depot haloperidol treatment*							
		Week 2	*Week 4*	*Week 6*	*Week 8*	*Week 10*	*Week 12*	*Week14*	*Week 16*
Hypokinesia	11 (3)	10 (3)	10 (2)	10 (1)	10	6 (1)	7	6	5
Rigidity	4	7 (2)	5 (1)	6	7	2	3	3	4
Tremor	3 (2)	5 (1)	6 (2)	3	5	4	1	2	1
Akathisia	2 (1)	3 (1)	3 (1)	1	2	1	1	—	—
Salivation	3	3 (1)	2	4 (1)	3 (1)	2	3 (1)	4 (1)	3 (1)
Somnolence	3 (1)	1	1	1	—	1	1	—	—
Depression	—	—	—	—	—	—	—	—	—

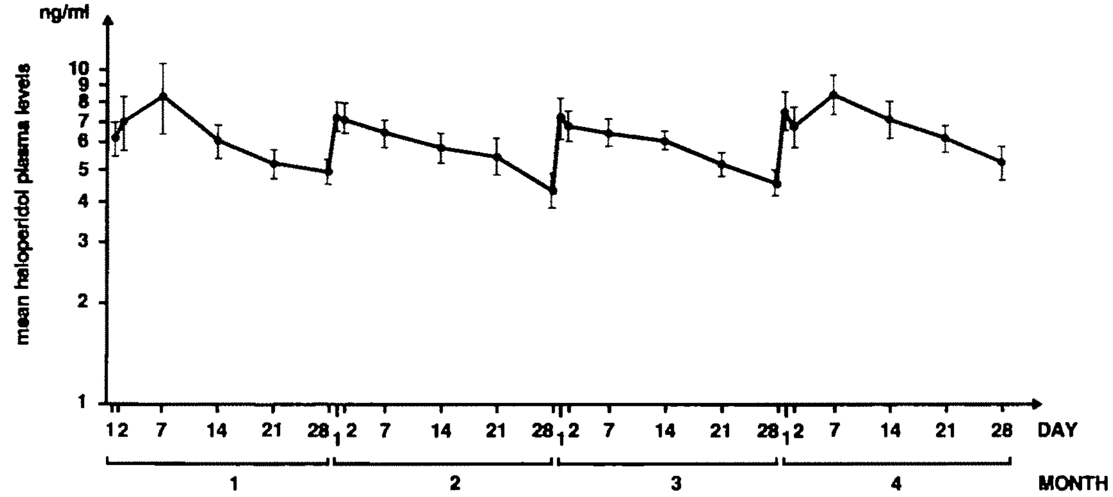

FIG. 3 Mean haloperidol plasma levels (±s.e.m.) adjusted to unit dosage of haloperidol decanoate. For clarity the measurements at 3 and 8 hours post-injection are not plotted. Months 1 and 2, $n = 19$; month 3, $n = 18$; month 4, $n = 14$.

There was no evidence that depot haloperidol decanoate treatment interfered with haematological and biochemical parameters.

3. Plasma drug levels

Correlation with dose

In patients receiving small doses, the mean plasma level varied between 2 and 5 ng/ml; patients with an intermediate dose had plasma levels between 4 and 7 ng/ml; while for the high-dose group, the range was from 8 to 16 ng/ml. There were considerable differences in plasma levels between individuals in the high-dose group, and to a lesser extent in the low- and intermediate-dose groups.

When the mean plasma levels of the whole group were standardised to a unit dose (200 mg for the loading dose and 100 mg for the subsequent injections), they only varied between trough and peak values of 4.2 and 8.4 ng/ml respectively. Peak values occurred between the first and seventh day (Figure 3). These plasma levels correspond quite closely to the haloperidol plasma concentrations during oral intake (mean 5.15 ng/ml, s.d. 2.75, for a unit dose of 10 mg haloperidol per day).

Calculation of the mean area under the curve (AUC) in Figure 3 for each of the four months of the trial showed a steady-state value from the first month onwards (Figure 4). The area under the curve (AUC) of the plasma-concentration/time graph can be used as an indication of bio-availability when blood levels for one drug are being compared and the elimination rate constant is not undergoing change.

In the whole series, the correlation between plasma level and dose was significant at the 0.001 level.

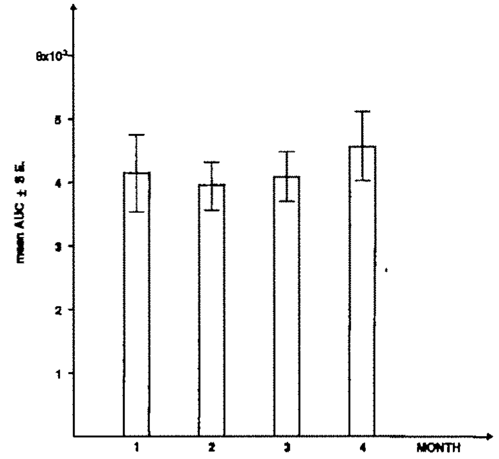

FIG. 4 Mean area under curve of plasma-level/time graph (Fig. 3) for each month of the trial. The AUC is an indicator of bio-availability.

Relation to clinical effect

To investigate the relation between plasma drug level and clinical effect, each patient was categorised each week, on the basis of her total BPRS score, as:

I unchanged or deteriorated
II moderately improved
III markedly improved

The BPRS evaluation was done on the same day as the blood sampling, and a t-test was used to compare plasma drug levels between groups I, II and III. The highest

TABLE III
Haloperidol plasma levels (geometric mean) of groups showing different degrees of clinical improvement (assessed by BPRS) at various stages of the trial

Therapeutic status	*Month 1*		*Month 2*		*Month 3*		*Month 4*	
	Day 14	*Day 28*	*Day 14*	*Day 28*	*Day 14*	*Day 28*	*Day 14*	*Day 28*
Group I—unchanged or deteriorated	5.9	5.0	6.0	4.1	7.6*	6.9	9.8	5.9
Group II—moderately improved	5.0	3.4	5.6	3.4	2.7	3.0	5.9	6.5
Group III—clearly improved	3.3	4.5	4.8	4.4	5.2	4.0	4.8	3.5

*Significant difference compared to group II: $P < 0.02$

plasma levels were found in the patients with least improvement, but the differences seldom reached statistical significance (Table III).

Because of an increase in psychotic symptoms in three patients at the end of the third month, their doses of haloperidol decanoate were increased by 50 or 100 mg. The deterioration in their clinical condition was not associated with a change in haloperidol plasma levels.

Discussion

Like the studies of De Buck *et al* (1981), Parent *et al* (1981) and Reyntjens *et al* (1982), the present investigation showed a very significant correlation between dose and plasma level.

Measurements of clinical condition with the BPRS and NOSIE-30 showed that about two-thirds of the patients were clinically unchanged or improved on both observation scales. The analysis of variance showed more pronounced improvement of scores on the NOSIE-30 scale, which monitors the social adaptation of the patient more closely than the BPRS does. In fact the cluster analysis suggested that clinical amelioration was due not to a diminution of psychotic thought, but to an improvement in social integration, with a lessening of hostility and amelioration of social competence. Only during the fourth month did the analysis of variance show a significant improvement of the total scores on both scales. This improvement paralleled a reduction of extrapyramidal symptomatology, but might also be explained by the fact that four patients who showed clinical deterioration at the end of the third month and so required more medication did not appear in the study population during the fourth month.

A significant correlation between haloperidol plasma level and therapeutic effect was seldom observed, although the plasma levels of the unchanged or deteriorated patients were generally higher than those of the clinically improved ones. This lack of correlation has been observed in other investigations: with the exception of a very weak correlation between these parameters for chlorpromazine (Rivera-Calimlim *et al*, 1973; Wode-Helgodt *et al*, 1978), it has so far been impossible to establish a consensus on the relation between plasma levels and therapeutic response to neuroleptics (Hollister, 1981). This holds true for both short-acting and long-acting neuroleptics, and may be due to protein binding and the high solubility of neuroleptic drugs.

We conclude that in our population of chronic patients, the administration of a loading dose of haloperidol decanoate offered no clinical advantages over the classical repeated dose (20 × daily oral dose): Deberdt *et al* (1980) obtained therapeutic results, comparable with those of this study, with chronic psychotic patients, without the use of a loading dose, and noted fewer side-effects at the onset of treatment.

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*H. De Cuyper, MD, PhD, *Psychiatrist and Scientific Collaborator, Academic Psychiatric Centre 'Salve Mater', Lovenjoel, near Leuven, Belgium.*

J. Bollen, MD, *Psychiatrist, Psychiatric Centre 'Sancta Maria', St Truiden, Belgium.*

H. M. van Praag, MD, PhD, *Chairman, Department of Psychiatry; Albert Einstein College of Medicine/ Montefiori Medical Centre, New York, USA.*

D. Verstraeten, PhD, *Coordinator of Scientific Research, Academic Psychiatric Centres, Leuven, Belgium.*

*Correspondence

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A Multivariate Investigation of Postpartum Mood Disturbance

P. R. GARD, S. L. HANDLEY, A. D. PARSONS and G. WALDRON

The interrelationships of 'blues' and later postpartum depression with a number of biochemical, medical, and psychosocial variables have been examined in 52 subjects. The two syndromes shared only an impressive association with a prior history of gynaecological problems. Puerperal 'blues' was characterised in addition by associations with primiparity, tearfulness during pregnancy, and reduced plasma total tryptophan in the early puerperium. Depressive symptomatology up to nine months postpartum was related to an excess of male births and to an altered pattern of decline of non-esterified fatty acids immediately postpartum. In each case, the 'risk' variables were statistically independent and combined linearly. Stepwise discriminant analysis successfully discriminated 'blues' and depression from their respective non-cases. 'Blues and postpartum depression were only weakly related and, apart from gynaecological history, each was associated with separate and independent causative factors.

The postpartum period is a time when significant increases in psychiatric disorder, especially of a depressive nature, are known to occur (Pitt, 1968, 1973). Apart from the appearance of frank psychosis, two non-psychotic disorders have been noted: a dysphoric state in the early puerperium ('blues') and an increased incidence of depressive symptoms in the ensuing months; these conditions have been reviewed in detail by Stein (1982) and by Kumar (1982). The relatively high incidence and predictable time of onset, particularly of 'blues' have prompted a number of prospective studies which have detected tentative links with the biochemical disturbances of parturition. Since these relationships have been found in separate studies, it is important to discover whether the same biochemical changes occur in all cases, which would suggest the likelihood of a single underlying cause. Medical and psychosocial factors have also been implicated in postpartum mood disorders (Kumar, 1982; Stein, 1982), but their influence in relation to biochemical factors has not been examined. The aim of the present study was therefore to examine selected biochemical, medical, and psychosocial factors, previously reported to be associated with mood disturbance, in a single sample of parturient women.

Among the biochemical variables, tryptophan was chosen for investigation because we have previously found (Handley *et al*, 1980) that the absence of the early postpartum peak in plasma tryptophan was associated with 'blues' and with the later occurrence of postpartum depression. Other studies have suggested that it is the non-albumin-bound fraction which is important (Stein *et al*, 1976; Handley *et al*, 1977), since this is the ultimate precursor of brain 5-hydroxytryptamine (5-HT) (Fernstrom & Wurtman, 1971). Entry of tryptophan into the brain is influenced by concentrations of large neutral amino acids in the circulation (Fernstrom & Wurtman, 1972); these were also examined. Non-esterified fatty-acids compete with tryptophan for albumin binding (Curzon *et al*, 1974), and have been found to be raised in endogenous depression (Van Praag & Leijnse, 1966). Among steroid hormones, changes in cortisol production have been identified in depression (Board *et al*, 1957) and, in a previous study (Handley *et al*, 1980), we found raised antenatal cortisol in 'blues' cases. It has been suggested that the sudden fall in progesterone at parturition may influence mood (Dalton, 1971), and progesterone has been used in the prophylaxis of postnatal depression (Dalton, 1982). Nott *et al* (1976) could detect slight differences in oestrogens but not in progesterone. Plasma 7,8-dihydrobiopterin, a cofactor in monoamine synthesis (Hosoda & Glick, 1966), was included because it is increased by antidepressant treatments (Leeming *et al*, 1982).

Method

The study took place at Birmingham Maternity Hospital, between the months of February and May. Subjects between 30 and 36 weeks gestation were invited to participate, provided they spoke English as their first language, were free from concurrent medical or psychiatric illness, and had not requested a 48 hour-admission.

Variables studied

At first contact, a medical and psycho-social history recorded age, nationality, marital status, and menstrual, gynaecological, and obstetric histories, together with psychiatric history of self and family. Details of present parturition, infant, and feeding mode were added after the delivery.

Emotional status was assessed by the Multiple Affect Adjective Checklist (MAACL, Zuckerman & Lubin, 1965) and Beck Depression Inventory, shortened form (BDI, Beck & Beamesderfer, 1974). Clinical interviews were all carried out by the first author. The antenatal interview was retrospective over pregnancy, and covered mood: depression, elation, lability, anxiety, irritability, and tearfulness were noted. Puerperal interviews (retrospective 24hr) looked for changes from antenatal scores, and also covered sleep, appetite, and feeding difficulties; nine months postpartum, the interviews covered all these aspects, with the addition of coping ability, fatigue, and retardation. Any special circumstances were included in the interview notes. Each variable was recorded as 0 (absent) to 3 (severe).

Plasma (stored at −30°C) was assayed by methods described by the following authors: total tryptophan (TP), Denkla & Dewey (1967) as modified by Bloxam & Warren (1974); free tryptophan (FTP) separation, Bloxam *et al* (1977); non-esterified fatty acids (NEFA), Curzon & Kantamaneni (1977); progesterone and oestradiol, Shaw *et al* (1974); oestriol, Evans *et al* (1981); 11-hydroxycorticosteroids. Mattingley (1962); dihydrobiopterin (DHB), Leeming *et al* (1982); amino acid analysis was carried out using a Locarte amino acid auto-analyser, samples were assayed for aspartic acid, threonine, proline, glycine, and the large neutral amino acids (alanine, valine, isoleucine, leucine, tyrosine, and phenylalanine).

Protocol

At the antenatal clinic, MAACL, BDI, clinical interview and venepuncture were performed between 36 and 38 weeks estimated gestation; MAACL, interview and venepuncture were carried out again on days 1 to 5 postpartum, with BDI on day 3. On the day of discharge, patients were asked whether they had heard of 'blues' (all had) and if so, whether they had experienced it this time. At a domiciliary visit, 9 months postpartum, women were again interviewed; those who were unavailable ($n=9$) completed a postal questionnaire containing the structured material of the interview. Diagnosis of 'blues' and postpartum depression was carried out from the rating scale and interview data before breaking the codes on the remaining variables.

Prior to venepuncture, subjects were required to avoid drugs known to affect plasma tryptophan binding and to eat a standard breakfast (cereal, toast and butter).

Statistical analysis

Nominal level variables were analysed by chi-squared and continuous variables by two-tailed t-test, unless otherwise stated. Since the large number of variables studied would increase the probability of detecting spurious relationships, stepwise discriminant analysis was used to confirm and extend the findings. This technique selects the combination of variables which best distinguishes between designated groups of subjects (Nie *et al*, 1975). It was used to discover which variables contributed significantly to discrimination of the 'blues' or depression cases.

Characteristics of the subjects

From a total of 65 women who were approached, 62 subjects agreed to participate. One withdrew antenatally, four were discontinued because of, respectively, obesity complicating venepuncture, emergency Caesarean section, neonatal death, and spina bifida infant; in five cases, occurrence of parturition was not reported within 24 hrs. The remaining 52 completed the study, and all but three were traced at 9 months; their mean age was 28.04 (range 17–36) years. Twenty-six subjects (50%) were primiparous; 40 (77%) were married, and two gave birth by Caesarean section. The mean duration of pregnancy was 39.8 (range 35–42) weeks; delivery was normally induced if pregnancy extended beyond 42 weeks. Thirty-four (67%) breast-fed their infants, 32 subjects gave birth to male infants. Eleven subjects reported previous gynaecological/obstetric problems (four infertile, four dilatation and curettage, one spontaneous abortion, one uterine 'growth', one antenatal admission).

Results

The 'blues'

Subjects were diagnosed as 'blues' cases if they demonstrated at least two of these values: MAACL (depression scale) >21; BDI >4 (low value due to shortened form); puerperal interview–positive change from antenatal; 'blues' self-report—positive. Fourteen subjects (27%) fulfilled these criteria; 28 (54%) were symptom-free and classed as non-cases. A further 10 (19%) were borderline in showing only one criterion (four subjects reported 'blues' only following their discharge from hospital; all four were already in the borderline category and were left there). There was excellent agreement between positive puerperal interview and 'blues' self-report.

When 'blues' cases were compared with non-cases, there were significant increases in previous gynaecological problems: 7 compared with 3 ($P<0.05$), antenatal tearfulness: 11 compared with 10 ($P<0.01$) and primiparity: 12 compared with 12 ($P<0.05$). As a group, the 'blues' cases showed a smaller rise in total plasma tryptophan on day 1 (Fig. 1).

These variables were independent of each other, and their combined incidence was strongly related to diagnosis (criterion for low day 1 tryptophan $\geqslant 10\,\mu g/ml$); thus, there was a strong linear relationship between the number of these factors present and case status (non-case, borderline, case): $r=+0.66$, $P<0.0001$.

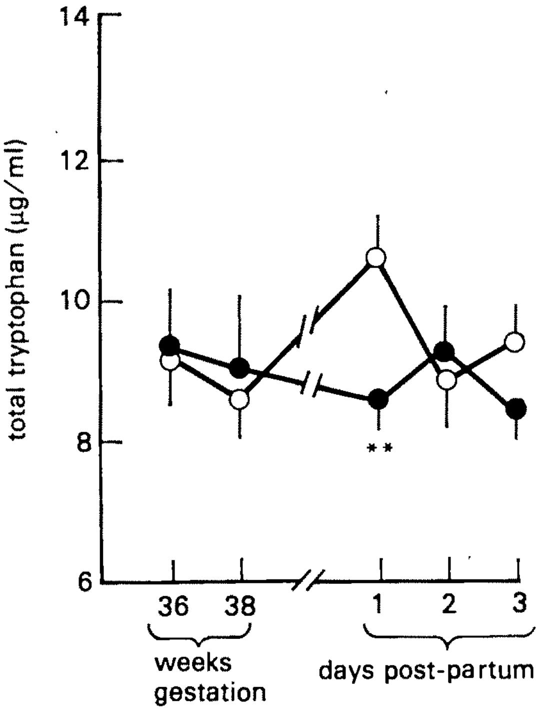

FIG. 1 Changes in total plasma tryptophan across parturition: comparison of cases and non-cases of 'blues'. Symbols represent group means for non-cases (○) and cases (●) of 'blues'. Vertical bars represent standard errors. [$**P<0.01$].

Discriminant analysis correctly classified 95% of non-cases and 90% of cases ($P<0.001$). The variables chosen by the analysis (Table I) included the above plus younger menarche and higher antenatal NEFA and progesterone as the discriminating characteristics of the 'blues' cases; these variables were not significantly related to each other (but see section on total tryptophan below).

Depressive symptoms

The interview material was assessed for evidence that a clinically important degree of depressive symptomatology had occurred between 1 week and 9 months postpartum, and had lasted at least 2 weeks; (for symptoms considered, see Method). In practice, the minimum duration found was 3 weeks, with a median of 8 weeks. Only those subjects considered by both PRG and GW (blind) to have shown unequivocal symptoms were included as cases. This resulted in 11 cases, two of whom had visited their general practitioner; a further 12 had shown some symptoms (borderline), and 26 (50%) had been entirely symptom-free; three were untraced.

Compared with the non-cases, the depression cases had more frequently reported gynaecological problems: 6 compared with 3 ($P<0.001$); later menarche 13.73 compared with 12.31 years ($P<0.001$) or had given birth to a male infant 10 compared with 14 ($P<0.05$). There was also an altered pattern of NEFA decline postpartum (Fig. 2) which was statistically significant (ANOVA, group/time interaction, $P<0.05$).

The number of these factors present was linearly related to case status ($r=+0.68$, $P<0.0001$); for this analysis, the best discriminating cut-off was used for interval level variables thus: menarche $\leqslant 13$ years, NEFA <0.38 meq/dm^3). The four variables were statistically independent.

TABLE I

Discriminant analysis of 'blues': variables which combined to distinguish 'blues' cases from non-cases

Step		*Wilks lambda (probability of change in lambda)*	*Standardised canonical discriminant function coefficient*
1	Parity (prim = 0, mult = 1)	0.797(0.0074)	−0.5532
2	Prior gynaecological problems	0.638(0.0009)	0.9234
3	Antenatal tearfulness	0.579(0.0008)	−0.5468
4	Postnatal total tryptophan (mean days 1–3)	0.498(0.0003)	−0.4761
5	Age of menarche	0.462(0.0004)	−0.7478
6	Antenatal progesterone	0.406(0.0002)	0.5491
7	Antenatal NEFA	0.380(0.0003)	0.3689

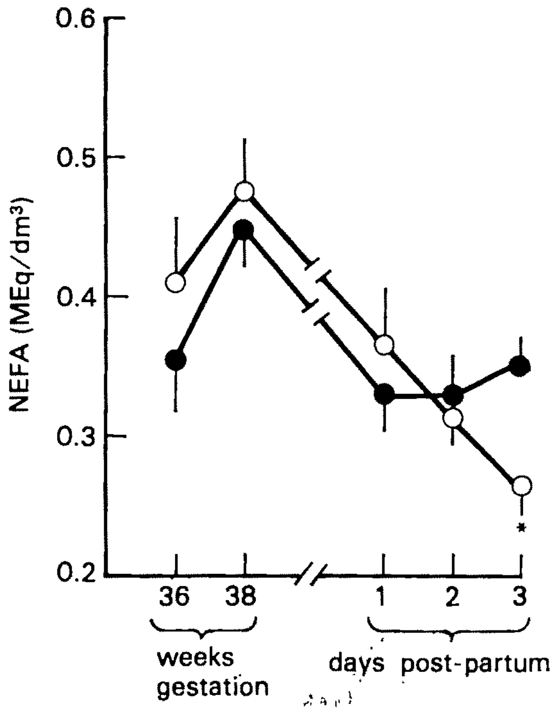

FIG. 2 Changes in plasma non-esterified fatty acids across parturition: comparison of cases and non-cases of later postpartum depression. Symbols represent group mean values for non-cases (○) and cases (●) of later postpartum depression. Vertical bars represent standard errors. [$P < 0.05$].

Discriminant analysis (Table II) was able to classify correctly all cases and non-cases of depression ($P < 0.001$) by selecting as case discriminators all the above variables plus multiparity, high antenatal cortisol, low antenatal oestriol and longer pregnancy. These variables were not related to each other, except for a weak *positive* correlation between cortisol and oestriol ($r = +0.32$, $P < 0.05$). The occurrence of 'blues' at the target parturition was also selected (see below).

The two subjects who had visited their general practitioner with a specific complaint of depression received antidepressant medication. One had had 'blues' and lacked the early tryptophan peak, while the other experienced the reverse; both had previous gynaecological problems.

Relationship between 'blues' and later depression

Five subjects experienced both 'blues' and depression, although this association was not statistically significant. Discriminant analysis for depression did, however, select 'blues' as having significant discriminating power (Table II). Although these five subjects were too small a group for analysis, it was noted that all had experienced gynaecological problems, together with menarche on or after 13 years. Four were primiparae, tearful antenatally, bore male infants, or had low puerperal total tryptophan, but each subject showed a different combination of these; three had raised puerperal NEFA.

Gynaecological/obstetric problems

Out of the 11 subjects with a history of such problems, five had both 'blues' and depression (see above); of these, two were previously infertile, a further two had undergone dilatation and curettage and one had suffered a spontaneous abortion. Two further subjects had experienced depression only (dilatation and curettage and previously

TABLE II

Discriminant analysis of postpartum depression: variables which combined to distinguish cases from non-cases

Step		*Wilks lambda (probability of change in lambda)*	*Standardised canonical discriminant function coefficient*
1	Age of menarche	0.790(0.032)	0.6169
2	Sex of infant (M = 1, F = 2)	0.751(0.067)	−1.3666
3	NEFA (postpartum day 3)	0.524(0.008)	0.6020
4	Prior gynaecological problems	0.292(0.0002)	0.9182
5	Parity (prim = 0, mult = 1)	0.246(0.0002)	1.3465
6	Length of this pregnancy	0.227(0.0004)	0.6112
7	Antenatal cortisol	0.203(0.0006)	0.9279
8	'Blues' (this pregnancy)	0.171(0.0007)	1.2454
9	Antenatal oestriol	0.137(0.0006)	−0.7497

infertile) and one only 'blues' (previously infertile). Of the remaining three, one was borderline for 'blues' and two for depression. Thus, none of these subjects was symptom-free.

Total plasma tryptophan

Total plasma tryptophan was related to both free tryptophan and NEFA, when each was measured on the same day. Total tryptophan showed a significant positive correlation with free tryptophan throughout ($r=+0.37$ antenatal; $+0.76$ day 1; $+0.27$ day 2; $+0.43$ day 3; $P<0.05$ on each occasion). The relationship of total tryptophan with NEFA was, however, only observed postnatally ($r=-0.29$ antenatal, NS; $+0.59$ day 1; $+0.32$ day 2; $+0.40$ day 3; $P<0.02$ for each postnatal day).

Despite these relationships, neither free tryptophan nor NEFA differed significantly in 'blues' cases, even on day 1 postpartum, the day of the early tryptophan peak (free tryptophan: cases 3.0 ± (s.e.)0.29 μg/ml, non-cases 3.27 ± 0.23 μg/ml; NEFA: cases 0.36 ± 0/04 meq/ml, non-cases 0.41 ± 0.05 meq/ml). Discriminant analysis failed to select postnatal free tryptophan or postnatal NEFA as significant discriminating variables, even when postnatal total tryptophan was omitted. In addition, there was no relationship between day 1 total tryptophan and antenatal NEFA, although both had discriminating power. Total tryptophan was correlated with oestradiol on day 2 postpartum and later (e.g. day 2: $r=-0.33$; day 3: $r=-0.38$; $P<0.05$), but not on day 1 postpartum, and there was no relationship between puerperal tryptophan and oestriol, progesterone or cortisol.

Unrelated variables

All other variables listed in the Methods were tested for their associations with 'blues' and depressive symptoms, and found to be unrelated. These variables also failed to contribute to the discrimination of cases of either 'blues' or depression.

Discussion

Postpartum 'blues' is not a strictly defined syndrome; this causes diagnostic problems and contributes to the varying estimates of its incidence (e.g. 5–80%, Hamilton, 1962; 50%, Pitt, 1973; 41%, Stein *et al*, 1981). We have used a method similar to the one we used previously (Handley *et al*, 1980), consisting of a combination of 'pencil and paper', verbal and observer-rated instruments, in order to detect the most clearly affected cases. The close agreement between the clinical rating of 'blues' and subjects' self-report shows that both subjects and observers must have been using very similar criteria. The observed incidence of 27% is, however, in the lower part of the reported range: addition of the borderline category brings the incidence up to 46%.

'Blues' cases, as diagnosed here, showed significantly lower values for plasma total tryptophan in the early puerperium. As with the majority of amino acids (Cox & Calame, 1978), circulating tryptophan is reduced during pregnancy, probably by a hormonal mechanism. Plasma tryptophan shows a biphasic rise over the first five days postpartum, and 'blues' sufferers have been reported to lack the early peak (Handley *et al*, 1980). The present study confirms this finding. That this is unlikely to be causative is shown by the failure of tryptophan supplementation to prevent the development of 'blues' (Harris, 1980); it is more likely to be a marker of some underlying predisposing mechanism (Handley *et al*, 1980). It therefore becomes important to trace what this mechanism might be. One way would be to find out what other biochemical changes occurred in association with 'blues' and low tryptophan. None of the other biochemical variables was associated with 'blues', when investigated individually, although raised antenatal NEFA and progesterone had significant discriminating power in the discriminant analysis. These differences were, however, independent of the low tryptophan.

Several studies have indicated the probable importance to depression of that portion of the circulating tryptophan which is not bound to albumin (free tryptophan; Yuwiler *et al*, 1977; Bloxam & Curzon, 1978) in contrast to our previous study, which implicated total tryptophan (Handley *et al*, 1980). However, it is possible that seasonal factors could produce a spurious association; we previously found that free tryptophan was at its lowest during the months when the incidence of 'blues' was high (Handley *et al*, 1980), and the present study was restricted to these months for that reason. It is only the free tryptophan which can enter the brain and generate 5-HT (Christensen *et al*, 1979), but in practice, this may not be of major importance because the uptake process has high affinity and can strip tryptophan from albumin (Yuwiler *et al*, 1977). The ratio of tryptophan to large neutral amino acids is probably more relevant because all share the same carrier for brain uptake (Fernstrom & Wurtman, 1972). Other studies have reported a reduced ratio in depression unrelated to childbirth (de Meyer *et al*, 1981). However, in the present instance, the ratio was no different in 'blues' cases from that found in 'normals' and it had no discriminating power, even when total tryptophan was omitted from the analysis. NEFA compete with tryptophan for albumin binding sites (Curzon *et al*, 1974), so it was not surprising that total tryptophan was related to both free tryptophan and to NEFA, when measured on the same day. However, these relationships were independent of the 'blues', and thus give no clue why 'blues' sufferers tend to lack the early tryptophan peak. Raised antenatal NEFA, although independent of reduced, puerperal tryptophan, did assist in the discrimination of 'blues' cases. This suggests that 'blues' sufferers might have been experiencing more stress antenatally. The implications of NEFA alterations are discussed more fully below.

It has been reported that women with the greatest fall in progesterone at parturition are also the most likely to report the 'blues' (Dalton, 1971, 1982; Nott, *et al*, 1976). We did not find any effect of the actual progesterone fall, although raised antenatal levels contributed to the discrimination of cases. How progesterone may be involved in mood changes is far from clear.

'Blues' subjects were also more likely to have experienced gynaecological problems; this has not previously been reported for 'blues', although women with depressed mood in later months were more likely to have been previously infertile (Kumar & Robson, 1978). Earlier menarche as a discriminator of 'blues' cases confirms the findings of Yalom (1968), and suggests the possible involvement of constitutional factors. Tearfulness is a common finding in 'blues' and should be used as a diagnostic criterion with care, since it is apparent from this and other studies that 'blues' cases cry more antenatally as well (Davidson, 1972; Nott *et al*, 1976; Handley *et al*, 1980, Stein *et al*, 1980).

Two previous studies (Yalom, 1968; Nott *et al*, 1976) found 'blues' more common among primiparae, while four (Pitt, 1973; Ballinger, 1979; Stein *et al*, 1981; Handley *et al*, 1980) did not. This would not be unexpected if primiparity is one rather weak contributor among several predisposing factors. Its incidence might well vary considerably over several relatively small samples.

The four variables individually associated with 'blues'—low puerperal tryptophan, primiparity, gynaecological problems, and antenatal tearfulness—were mutually independent, and the likelihood of 'blues' increased linearly with the number present. 'Blues' thus appears to be associated with multiple causative factors.

Symptoms of depression are frequent in the months following childbirth (Pitt, 1968). In our previous study, we used a simple criterion for postpartum depression, i.e. a visit to a general practitioner with a specific complaint of this nature. However, this may have resulted in under-reporting, in that by no means all sufferers complain to their doctor (Kumar & Robson, 1978). The occurrence of depressive mood change was therefore sought by retrospective interview (or questionnaire in those otherwise inaccessible). Only those subjects with clear evidence of depression since the birth, in the opinion of the interviewing psychologist and of a psychiatrist working from the interview data, were selected as cases. This gave an incidence of 21%, which is high compared with previous studies (Pitt, 1968; Dalton, 1971; Kumar, 1982), although not substantially above the 17% recorded by Paykel *et al* (1980). Only two of these cases fulfilled our previous criterion—too few for a separate statistical analysis. The cases were contrasted with symptom-free subjects: the only biochemical difference between these two groups was an altered pattern of NEFA decline.

NEFA tend to be raised antenatally and to decline at parturition (Burt, 1960). Endogenous depressives have been reported to show exaggerated rises in NEFA following mild stress (Curzon *et al*, 1979). The failure of NEFA to decline as rapidly postpartum in subjects who went on to become depressed might indicate a greater reactivity to the stress of parturition. Alternatively (or in addition), these subjects may differ in tissue glucose handling. Elevated NEFA in endogenous depression is likely to be due to an impairment of triglyceride synthesis, caused by impaired uptake of glucose (Pryce, 1958; van Praag & Leinjse, 1966; Mueller *et al*, 1970). The finding of impaired NEFA decline in the puerperium might indicate that this is a constitutional difference, detectable at a time when there is no overt change in mood. Lowered antenatal oestriol also had discriminating power in distinguishing the depression cases. Oestriol is produced by the foetal adrenal, but no subject had values low enough to suggest an endangered foetus.

A positive gynaecological history appeared to be an important predisposing factor for depression; an association of previous infertility or abortion with postpartum depressive symptoms has been described previously (Kumar & Robson, 1978). Intuitively, it could be predicted that the emotional implications of a successful pregnancy might be particularly intense for such subjects, but constitutional factors cannot yet be ruled out. The relevance of gynaecological history clearly requires further investigation, since it could be an easily obtained indicator of women at special risk.

Birth of a male infant was a novel finding of unknown significance, as was the detection of longer pregnancy as a discriminating variable for depression. As with 'blues', the variables detectable by their individual associations were additive in defining the risk of suffering depressive symptoms, again underlining the importance of multiple causation.

There was comparatively little overlap between the occurrence of 'blues' and of later postpartum depression, and this overlap was at chance levels, although 'blues' did make a significant contribution to the discrimination of cases of postpartum depression. Apart from a positive gynaecological history, each condition was associated with separate risk factors, and the group with both conditions had the risk factors associated with each. It was interesting that all subjects in the group with both 'blues' and depression had experienced the only common risk factor of positive gynaecological history. However, the inclusion of both gynaecological history and 'blues' in the combination of variables which best discriminated depression cases shows that each must have contained information not contributed by the other (Nie *et al,* 1975). Thus, this study does to some extent confirm previous investigations, which have reported a significant overlap (Pitt, 1968, 1973: Paykel *et al,* 1980; Dalton, 1971). Nevertheless, the two conditions were biochemically dissimilar.

The lack of the early tryptophan peak in 'blues' cases (Handley *et al,* 1980) has been confirmed by the present study, but this was not associated with subsequent depressive symptoms. The previous criterion of a visit to a doctor with a specific complaint of depression was fulfilled by only two subjects: one with early tryptophan peak present who did not experience blues, and one with the peak absent, who did. This study has therefore generated insufficient data to confirm our previous finding that low puerperal tryptophan was associated with subsequent complaints of depression. It does, however, seem clear that disturbance of puerperal tryptophan regulation is not a feature of the type of depressive symptomatology used here for case diagnosis. Raised cortisol, or altered secretory patterns are well known in endogenous depression (see Handley *et al,* 1980). We have reported raised antenatal values in 'blues' cases, but there was no association with later depression (Handley *et al,* 1980). We have reported raised antenatal values in 'blues' cases, but there was no association with later depression (Handley *et al,* 1980). In the present study, there was no significant difference in antenatal cortisol in either group, although raised antenatal cortisol did contribute to the discrimination of depression.

Thus, this study provides partial confirmation of our previous work, in that there appears to be a disturbance in the regulation of plasma tryptophan during the early puerperium in subjects who experience 'blues'. However, it was not possible to confirm whether this extended to later postpartum depression, severe enough to give rise to consultation of a general practitioner. The tryptophan disturbance appeared to be independent of the other biochemical, medical and psychosocial variables measured.

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P. R. Gard B.Sc, PhD, *Lecturer in Pharmacology, Department of Pharmacy, Brighton Polytechnic, Moulsecombe, Brighton.*

*Sheila L. Handley, BPharm (Lond), PhD, *Lecturer in Pharmacology, Drug Mechanisms Research Unit, Department of Pharmaceutical Sciences, University of Aston, Birmingham.*

A. D. Parsons, MB, BS, MRCOG, *Lecturer in Obstetrics and Gynaecology, University of Birmingham, Edgbaston, Birmingham.*

Gillian Waldron, MB, ChB, MRCPsych, *Lecturer in Psychiatry, The London Hospital Medical College, London E1.*

*Correspondence

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The Prevalence of Schizophrenia in a Remote Area of Botswana

DAVID I. BEN-TOVIM and JOSEPHINE M. CUSHNIE

We ascertained the one-year prevalence of schizophrenia amongst individuals aged 15 years or older living in six villages in a remote area of Botswana. All cases were diagnosed independently by two experienced psychiatrists, following ICD9 rubrics. DSM-III criteria were also applied, separately. Accurate contemporary population estimates of the villages were available. The age-adjusted prevalence of schizophrenia was 5·3 per 1000 in terms of ICD9, or 4.3 per 1000 by DSM-III, which has an upper age limit for onset of 45 years. These figures are well within the range generally reported for industrial communities. Remote village life in Botswana appears to offer no protection against the development of schizophrenia.

Is the prevalence of schizophrenia constant with respect to time and place? Torrey (1980) has recently proposed that schizophrenia is a disease of industrialised society, thus reviving an argument that in a broader form has been alive for at least 150 years (Morison, 1824; Burrows, 1828; Maudsley, 1879). Torrey, and more recently Hare (1983), have reviewed diverse historical data and concluded that there may have been a real increase in insanity in the nineteenth century. Torrey (1980) has also used contemporary fieldwork studies to examine geographical variations in the prevalence of schizophrenia, and has identified a relative failure of schizophrenia to penetrate to the more remote parts of certain developing countries such as Papua New Guinea. Murphy (1984) has also said of schizophrenia that "with some notable exceptions, such as the rural Irish . . . its prevalence is higher in more civilized societies than in more primitive ones . . . "

Both Torrey and Hare cautiously espouse a viral transmission theory to explain both the temporal and the geographical variations in the prevalence of schizophrenia, but the study of its prevalence is also of interest to those who favour a gene–environment aetiology. If schizophrenia is less common in non-industrialised settings, it could be hypothesised that people who are genetically predisposed to schizophrenia are more likely to break down when they are subject to the stress of modern industrial society. Identifying the relevant stresses might then give clues to prevention and management.

Factual information from the African continent is relevant to this debate; but it is scanty, despite the fact that between 70% and 80% of Africans continue to live in rural communities. Much of Africa is under-developed by Western standards, although it would be wrong to see even the more remote parts of Africa as being completely sequestered from modern life. Agrarian communities in Africa have been heavily affected by broad economic and social forces in both the colonial and the post-colonial periods; and unprecedented population growth has, in modern times, led to exceptional periodic privation. Nevertheless, there are many parts of Africa which contain societies that come as close as anywhere on earth to ideal testing-grounds for Torrey's theory that schizophrenia is a product of industrialisation.

Schizophrenia has been repeatedly identified in various parts of Africa by both clinical methods (German, 1972) and structured interviews (World Health Organisation, 1973; Orley & Wing, 1979). However, specific studies of prevalence have either lacked an accurate contemporary population base (Field, 1968; Sikanartey & Eaton, 1984) or have not involved active case-finding within the general population under investigation (Sikanartey & Eaton, 1984). We now report a study from a remote area of Botswana that avoids these pitfalls.

Method

Botswana is a land-locked sub-Saharan African country. Its population of one million is scattered across a land-mass of 570,000 square miles. The terrain is harsh, being mainly composed of the Kalahari Desert. *Per capita* income at the time of the study was approximately US$270 *per annum* (Ministry of Finance & Development Planning, 1980), and child mortality during the first two years of life was 132 per 1000 live births (Ministry of Health, 1979). Botswana is a 'least-developed nation' by U.N. criteria.

The present study was conducted in six small villages in the Chobe region of Botswana. Chobe occupies an area of approximately 20 000 square kilometres in the far north of the country. It lies approximately 1000 kilometres from Gaborone, Botswana's capital city, and at least half of Chobe's only access road is unsurfaced. Five of the villages under study were one day's drive to the west of Chobe's administrative centre, which is the township of Kasane, and the remaining village was a similar distance to the east. Four-wheel-drive vehicles and local guides were required to reach all the villages.

There is no industrial activity whatsoever in the Chobe region, and the inhabitants of the villages we studied live almost entirely by subsistence farming, cattle-rearing, and fishing. There is no telephone system, water-supply system, electricity, or other modern amenity in any of the villages. There are a small number of international visitors to the Chobe National Park, which lies within the region. These visitors almost never penetrate to the study villages, as there are no clearly-laid-out roads for them to follow. Although there are regular contacts between the villages and Botswana's national administration, founded after political independence in 1966, the villages' tribal organisation and tribal lifestyles have remained fairly untouched by the more modern political and social developments in the rest of the country. However, primary schools have recently been established throughout the region, and the pace of change will undoubtedly increase.

The villages were chosen for study because they were the most remote settlements that were regularly visited by the authors: they comprised all the substantial village settlements in the Chobe region. The present investigation was conducted over a period of one year, from June 1981 to June 1982. Each of the six villages was visited four times during that period. The visits took one week each and were at regular intervals; they formed part of a remote-area psychiatric service which has been described elsewhere (Ben-Tovim, 1983, 1984; Ben-Tovim & Kundu, 1982). Careful records were kept by the authors during each visit, as described below. However, the visits were not specifically undertaken to study the prevalence of schizophrenia.

In each village, the study team linked up with the local village health-worker (Ben-Tovim & Kundu, 1982; Ben-Tovim, 1984). These workers were forewarned of our arrival and acted as key informants, identifying all those people in their communities whom they knew to be mentally disturbed. Other key informants, including tribal authorities, community workers, traditional healers, religious healers and school teachers, were also consulted. Patients and their families were also asked if they knew of any other individuals with disorders similar to their own.

All those people that were identified by any informant as suffering from some kind of mental disturbance were located and seen, either in the village health post or in their homes. Treatment was given if necessary. Efforts were made to follow-up all patients during subsequent visits.

Diagnostic interviews were conducted jointly by the two authors, who are both experienced European psychiatrists and had been practising as specialist psychiatrists in Botswana for 12 months prior to the beginning of the study. Each of us noted down details of the patients, following a semi-structured interview format. The data gathered included demographic details and clinical descriptions.

One of us (D.I. B-T) was the Superintendent of Botswana's sole mental hospital (located near the capital) at the time the study began. A one-day census of all patients under treatment in that hospital was conducted by D.I. B-T in June 1981, and the normal place of residence of each patient was identified. Admissions to the hospital were monitored during the study period, as were in-patient admissions to a four-bed psychiatric unit in a general hospital that lay mid-way between Chobe and the State Mental Hospital. The general hospital psychiatric unit started admitting in-patients in April 1982.

A national population census was conducted by the Botswana Government three months before the start of our study. The study villages were included in this census, which involved trained enumerators and extensive cross-checks on reliability and comprehensiveness of data-gathering (Census Office, 1982). Published contemporary information was therefore available by which to determine the size and composition of the populations of the villages under study, and there was every reason to believe that the population data were accurate. Patients were considered eligible for entry into the study if they had been resident within the census boundaries of the village for six months prior to assessment and were at least 15 years-old.

The indigenous peoples of the part of the Chobe region under investigation come mainly from the Subiya tribal group, and all the villages studied were tribally homogeneous. Interviews were conducted in the national languages (English and Setswana) and in the local dialect. The psychiatric nurses who were part of the study team were bi- and tri-lingual. They were familiar with both indigenous and Western concepts of mental disorder, and were well known to the authors: they acted as interpreters when necessary. Information was sought from family members and all other available sources whenever possible. Both authors had been trained in the European ('narrow') tradition of diagnosing schizophrenia (Cooper *et al*, 1972). Diagnoses on all patients seen were recorded separately by the two authors, each using both ICD-9 rubrics and DSM-III criteria separately. A field study, reported elsewhere, has shown DSM-III to be applicable in Botswana (Ben-Tovim, 1985). In the event of differences, a final diagnosis was to be reached by consensus; in fact this problem never occurred. All patients were also seen by a Regional Medical Officer who accompanied us on our trips.

Results

The age-distributions of the populations of many developing countries are markedly skewed, compared with populations in the developed world. Developing countries have a far larger proportion of young and very young people; so to make comparisons between countries more meaningful, it is conventional to adjust prevalence figures to the age of maximum risk, i.e. 15 years and older (Leff, 1981). The villages we studied ranged in size from 256 inhabitants to over 600: the total population of the six villages was 2526. In Botswana as a whole, 56% of the population was aged 15 years or older at the commencement of this study (Census Office, 1982), and 2% of the younger ones entered their fifteenth year during the study period. In our six villages, the total population aged 15 or over during the study period was found to be 1133.

In all, 26 patients were seen in the villages at some time during the study period. Of those, six were confidently diagnosed by both authors as fulfilling ICD9 criteria for schizophrenia. All six also fulfilled the DSM-III clinical criteria, except that the age of onset of one patient was more than 45 years. There were no disagreements between the authors on the diagnosis of the six schizophrenics. In a further two cases, both authors diagnosed psychosis but neither made a diagnosis of schizophrenia. One of these patients exhibited a syndrome involving disturbed behaviour and a wide variety of abnormal movements, which seemed post-encephalitic in nature: the other abused alcohol very heavily. There were thus no cases in which one of us made a diagnosis of schizophrenia and the other disagreed.

Brief case histories of all six index cases are given in the Appendix below. The illnesses described were severe and of extended duration. No laboratory tests were performed on these patients, but all were reviewed by the Regional Medical Officer, who thought it unlikely that any were suffering either from local tropical disorders or from malnutrition of sufficient severity to explain the current disorders.

No patients from the study area were found amongst the residents of the State Mental Hospital during the census conducted there at the outset of the study, and no patients from the study area were admitted to the State Hospital, or to the general-hospital psychiatric unit, during the study year.

On the basis of ICD9, the one-year prevalence of cases of schizophrenia for the population of the study area aged 15 years or older was 5.3 per 1000 of the population. Using DSM-III criteria, which have an upper age-limit for the onset of schizophrenia, gave an age-related prevalence of 4.3 per 1000 of the population.

Discussion

Direct comparison of our work with other studies in the developed world may not be appropriate, because it is not clear that identical diagnostic criteria have been universally applied. Nevertheless, our figure are well within the ranges found for the inner urban areas of London (Leff, 1981), Munroe Country in New York (Babigian, 1975), Canadian villages (Murphy, 1982), urban Sweden (Haudin, 1984) and elsewhere in the developed and the developing world (Leff, 1981). However, they stand in contrast to the low prevalence (0.8 per 1000) reported by Sikanartey & Eaton (1984) for an urban area of Ghana. Their figure was for point prevalence, but as all the cases we found in the present investigation were chronic disorders, our annual and point prevalences were unlikely to have been substantially different. However, Sikanartey & Eaton (1984) relied on surveying current attenders at health facilities, without actively searching for cases in the community. If we had used that method alone, it would have appeared that schizophrenia did not occur at all in the area under study: case-finding using key informants made the real picture more apparent.

There are two major defects in the design of our study. Firstly, a relatively small population was surveyed, and any slight alteration in the absolute number of index patients would have greatly affected the prevalence figures. Secondly, we did not use standardised interviewing techniques: this was an unfunded study by service workers, and the translation and field-testing of the available structured interviews was beyond our resources. An attempt was made to minimise any error resulting from this clear deficiency by ensuring that all diagnoses were made independently by two experienced psychiatrists, both of us trained in a European 'narrow' tradition of diagnosing schizophrenia. We were both also familiar with the presentation of psychiatric problems in Botswana. We believe the estimates reported here to be conservative, but clearly our results cannot be viewed as definitive.

There is nowhere in Botswana that is completely untouched by modern life. Nevertheless, in comparison with many other parts of black Africa, Botswana's social systems have remained fairly intact (Comaroff, 1977; Alverson, 1978), and the patients described here lived within African villages that were tribal and rural in character. The villages lacked any kind of modern communications or industrial infrastructure, but there was no evidence that such a setting provided any protection against the development of schizophrenia.

Acknowledgements

The field work for this study was conducted while both authors were consultant psychiatrists to the Ministry of Health, Republic of Botswana. This report was partly prepared while Dr Ben-Tovim was Wellcome Research Fellow at the Institute of Psychiatry, London. We gratefully acknowledge the assistance of Dr Alain Le Vigoreaux, formerly Resident Medical Officer, Chobe, Botswana.

Appendix: Case Histories

Case 1. A 60-year-old married woman, who had had no formal education, presented with a one-year history of periods of muteness and withdrawal, alternating with episodes of disturbed behaviour. When disturbed, she expressed delusions that people wished to kill her, and ran away from her family. Thought disorder was prominent at examination. She responded well to phenothiazines. (ICD9 295.2).

Case 2. This 30-year-old man, who had never worked nor attended school, had spent three years as an in-patient at the State Mental Hospital. After his discharge in 1979 he remained aggressive and violent, and tended to hide in the bush surrounding his village. When seen, he showed impoverished speech and blunted affect. With phenothiazine maintenance treatment, his behaviour became more manageable, and he stayed within the village. He remained disordered in speech and thought. (ICD9 295.6)

Case 3. This 26-year-old man had had two 3-month periods in the State Mental Hospital within the last ten years. His illness began while he was a secondary-school student. His relatives gave a consistent history of a variety of delusions and auditory hallucinations at the time of onset of the disorder. When seen by the authors, the patient had gradually relapsed into a silent, withdrawn, and blunted state. He remained that way during our first two visits, but with continuous phenothiazine treatment became more active and talkative. However, his speech was never easy to follow (ICD9 295.6)

Case 4. A 55-year-old man presented with a 30-year history of abnormal behaviour. Several informants gave a consistent story of long periods during which the patient would wander through the village shouting out loud, appearing to converse in response to hallucinatory voices. During these times, he feared the company of others. He had been dismissed from a responsible position with the police because of his behaviour. Once on phenothiazine, he was able to resume his social and family obligations, and his behaviour became more normal. (ICD9 295.3).

Case 5. When this 34-year-old married woman was first seen, she presented with an unclear past history of psychiatric illness, and a history of neurotic symptomatology and vague visual hallucinations during the previous 12 months. During a subsequent visit, she had to be untied by the authors from a tee to which she had been tethered for some days; it appeared that she had been trying to injure members of her family for a number of weeks. At interview, she described a variety of auditory hallucinations, which included threats to hurt and harm her, and she also believed that members of her family were involved in a plot to kill her. She had never been formally employed and had received no schooling. Her speech was at times hard to follow. She made a good initial response to phenothiazines, but was then lost to follow-up. (ICD9 295.3)

Case 6. A 40-year-old uneducated married woman presented with a one-year history of experiencing various ancestral voices, addressing her and conversing between themselves. She also experienced tactile hallucinations of a crawling sensation under her skin. She had found it hard to attend to her domestic duties during the past year, but there had been no overt behavioural disturbance, and her speech was normal in form. There was little response to phenothiazines, and her experiences persisted unchanged during the survey period. Careful physical examination revealed no organic cause for her complaints. (ICD9 295.9).

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*David I. Ben-Tovim, PhD, MBBS, MRCPsych, *Director Department of Psychiatry, Repatriation General Hospital, Daw Park, South Australia 5041: Senior Lecturer, Flinders University of South Australia.*

Josephine M. Cushnie, MBBS, MRCPsych. *Specialist Psychiatrist, Drug and Alcohol Services Council; Clinical Lecturer, Flinders University of South Australia.*

*Correspondence

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Development of Scales to Measure Treatment Attitudes in Psychiatry

GREG WILKINSON and PAUL WILLIAMS

We used multiple regression analysis to modify and shorten two scales for measuring practitioners' attitudes to psychotherapy and drug therapy. The resulting scales have been combined in a 21-item questionnaire (Treatment Attitudes in Psychiatry Scales (TAPS)) which is brief and easy to use, and should have wide application in psychiatry. The results of a concurrent validation of the scales, using two large groups of consultant psychiatrists who were members of either the Biological Psychiatry or Psychotherapy Section of the Royal College of Psychiatrists, show the extent to which their attitudes to psychotherapy or drug therapy tend to overlap. Polarisation of attitudes was more evident in the results from the Biological Psychiatry Section. A method is described by which scores obtained with the TAPS can readily be compared with those obtained by the criterion groups.

Attitudes to treatment are a potential source of bias in the assessment of both medical and psychiatric interventions, but little attention appears to have been paid to the questions whether, and to what degree, clinicians' attitudes to treatment may affect outcome. This is true both in psychiatry, where much attention has centred on the problems surrounding diagnostic reliability, and in general practice, where there are wide differences among doctors in their recognition, treatment, and referral practices for patients with psychiatric disorders (Wilkinson, 1985). It is acknowledged that comprehensive attempts to study these variations require account to be taken not only of practitioners' professional characteristics, but also of their personal characteristics, and, in particular, their attitudes to psychiatry. The most important practical aspect of psychiatry concerns patient management, and there is a clear need for an instrument to measure doctors' treatment attitudes. Such an instrument, if brief and simple in use, would have application in studies to evaluate treatment (by specialist psychiatrists as well as primary care physicians) and also in training.

At present, there are few instruments designed for this purpose (Mason & Sacks, 1959; MacAndrew & Rosen, 1964; Caine & Smail, 1966). The most widely known, the MacAndrew and Rosen psychotherapy and drug therapy scales, are complicated, time-consuming, and do not appear to have been validated adequately. The only study we have identified (Lipman *et al*, 1970) interpreted data obtained from observations on 12 psychiatrists as being supportive of the validity of the drug therapy scale alone.

For these reasons, we decided to simplify and validate the scales for general use, using a statistical approach based on multiple regression analysis.

Background

Both of the MacAndrew & Rosen scales consist of 21 items. Subjects allocate the items comprising each scale along a seven-point continuum, from 'least agreed with' to 'most agreed with'. To ensure maximum inter-item discrimination, subjects are then required to make their allocation of items conform to a rectangular distribution so that, when all items have been allocated, three are contained in each of seven scale categories. Those three items with which a given subject least agreed are placed in category number one, and those with which he most agreed are placed in number seven. For each subject, a score is assigned to each of the 21 items, equal to the category in which the subject places it. The resulting array of 21 scores is then correlated with the array of 21 'absolute favourability scores' previously obtained from six independent judges. The magnitude of the correlation coefficient is then taken as the subject's score on that scale, and his relative preference for one treatment modality or the other is taken as the difference between his correlation scores on the two scales.

This is clearly a complicated procedure, which is neither easy to administer nor to complete. The authors found no predictable relationship between the two therapeutic attitudes for their total sample: the results were said to demonstrate the face validity of the two scales when they were presented separately, and to provide relative discriminations when they were used conjointly.

TABLE I
Characteristics of criterion groups

	Biological psychiatry	*Psychotherapy*
Male	113	89
Female	12	22
Mean age	47 years	48 years
Response rate	87%	72%
Medical qualification		
UK	68%	80%
Elsewhere	32%	20%
Mean years' of medical qualification	21 years	23 years
Place of work		
London	43%	66%
Elsewhere in UK	57%	34%
Type of patients		
Adults	92%	90%
Children	8%	10%
Academic post*	15%	19%
Publications*	39%	59%
Higher degrees of diplomas*	45%	36%

*Minimal estimates, taken from *The Medical Directory*.

Method

Modification of the MacAndrew and Rosen scales

We constructed a 42-item questionnaire by combining and randomising the statements of therapeutic attitude from the two 21-item scales. Small changes were made to the wording of each statement for consistency. Each statement was followed by a 10 cm visual analogue scale, anchored at one end by 'strongly agree', and at the other end by 'strongly disagree'.

Subjects

We chose two criterion groups. For the psychotherapy scale, the group consisted of consultant psychotherapists who were members of the Psychotherapy Section of the Royal College of Psychiatrists. The criterion group for the drug therapy scale consisted of consultant psychiatrists who were members of the Biological Psychiatry Section. The entire sample from the Psychotherapy Section was selected for inclusion in the study, as was a random half of the Biological Psychiatry sample.

Description of criterion groups

The groups were comparable (see Table I): 70 respondents from the psychotherapy group indicated that they predominantly practised psychodynamic psychotherapy, while 12 practised some other form of psychotherapy. Of the drug therapy group, 61 respondents considered themselves to be predominanly biological in psychiatric orientation, whereas 45 did not. In each case, there were seven non-respondents.

Data collection

The modified 42-item questionnaire incorporating all the MacAndrew & Rosen statements was sent by post to both groups in the summer of 1984, with an explanatory letter.

Measurement and rescaling of visual analogue scale responses

The visual analogue responses obtained were measured in millimetres. Depending upon the majority response of the group concerned, each psychotherapy and drug therapy item was scored positively from one or other end of the analogue scale. The data were then divided into five categories (scores 0–20 = 2, 21–40 = 1; 41–60 = 0; 61–80 = −1; and 81–100 = −2; or *vice versa*).

In this way, a psychotherapy score could be calculated for each member of the psychotherapy group by summing the values on the psychotherapy items. Similarly, a drug therapy score could be calculated for each of the biological psychiatry group by summing the values on the drug therapy items.

Results

Preliminary selection of psychotherapy and drug therapy items for further analysis

Student's t-tests and discriminant function analyses were performed on the 42-item questionnaire data obtained from each criterion group, to find: (i) psychotherapy items which discriminated between those who predominantly practised psychodynamic psychotherapy ($n=65$) and those who practised other forms of psychotherapy ($n=68$); and (ii) drug therapy items which discriminated between those who did ($n=57$) or did not ($n=43$ indicate a predominantly biological psychiatric orientation. Only those who provided complete data were included in this analysis.

This was done in order to discard those items which discriminated between the above sub-groups, and to retain the largest possible criterion groups. For our purposes, a decision was taken to adopt a one-in-a-hundred probability level as indicating statistical significance.

Two psychotherapy items and two drug therapy items were excluded on these grounds, and all subsequent analyses were conducted with the 38 remaining items.

Reduction of scales

In order to shorten the psychotherapy and drug therapy scales, multiple regression analyses were performed separately on the data obtained from each of the criterion groups: (i) a psychotherapy score (PS) was calculated for

TABLE II

Scores on reduced psychotherapy and drug therapy scales

Criterion group	*n**	*Median*	*Range*	*Mean*	*SE*
Psychotherapy					
RPS	73	22	5–33	21.8	0.7
RDS	75	19	−6–33	17.9	1.1
Drug therapy					
RPS	105	13	−10–30	12.7	0.8
RDS	104	28	0–37	26.6	0.6

Scores on reduced psychotherapy and drug therapy scales in quartiles

	Minimum	*First*	*Median*	*Third*	*Maximum*
Psychotherapy					
RPS	5	18	22	26	33
RDS	−6	10	19	25	33
Drug therapy					
RPS	−10	8	13	18	30
RDS	0	23	28	31	37

*Sample sizes differ within sub-groups due to missing values.

the psychotherapy group by summing the scores from each of the psychotherapy items. A drug therapy score (DS) was calculated for the biological psychiatry group in the same way; (ii) these PS and DS scores became the dependent variables in separate multiple regression equations. In each case, the predictor variables were the respective 19 individual psychotherapy or drug therapy item scores.

The results were that: (i) *for the psychotherapy criterion group*, the scores from 11 items on the psychotherapy scale together accounted for 90% of the variance in PS; and (ii) *for the biological psychiatry criterion group*, the scores from ten items on the drug therapy scale together accounted for 91% of the variance in DS. These 21 items (11 psychotherapy and ten drug therapy) were chosen to form the: *Treatment Attitudes in Psychiatry Scales (TAPS)* (see Appendix).

Scores obtained by criterion groups on reduced psychotherapy and drug therapy scales (TAPS)

Revised psychotherapy and drug therapy scores (RPS and RDS, respectively) were calculated for each criterion group, using the scores from the above 11 psychotherapy and the ten drug therapy items (Table II).

Concurrent validation

The psychotherapy group's RPS and RDS scores were then compared with those of the biological psychiatry group, using the median test (Table III). Although our main interest was not to discriminate between the two groups in terms of these scores, we expected to find that the psychotherapy group would score higher on RPS, and that the biological psychiatry group would score higher on RDS.

In fact, there was a significant difference between the criterion groups in their RPS scores ($\chi^2=40{\cdot}9$; d.f. = 1; $P<0{\cdot}001$), the psychotherapy group having the higher median score. Similarly, there was a significant difference between the groups in their RDS scores ($\chi^2=31{\cdot}3$; d.f. = 1; $P<0{\cdot}001$), the biological psychiatry group having the higher median score. There was a greater tendency towards polarisation of attitudes (as judged by RPS and RDS scores) in the biological psychiatry group than in the psychotherapy group.

Plotting of scores and transformation of data

To make the scores more meaningful, we wished to express an individual's RPS or RDS score in terms of the proportion of the respective criterion group achieving such a score; e.g., an individual's RPS score could then be quickly related to the distribution of such scores in the psychotherapy group. For each criterion group, graphs were drawn: the coordinates were (i) the individuals' respective RPS or RDS scores; and (ii) the cumulative percentages of these scores. Both curves were sigmoid in shape, with straight-line central portions. An attempt was now made to straighten out the curves by transformation of the cumulative percentage data. Logistic, arscine, and probit transformations gave similar results. When the chi-square goodness-of-fit test was applied to estimated cumulative

TABLE III
Comparison of criterion groups' scores

	Revised Psychotherapy Score (RPS)		
	Biological Psychiatry	*Psychotherapy*	*Total*
Scores above combined median	31	58	89
Scores below combined median	74	15	89
Total	105	73	178

	Revised Drug Therapy Score (RDS)		
	Biological Psychiatry	*Psychotherapy*	*Total*
Scores above combined median	71	19	90
Scores below combined median	33	56	89
Total	104	73	179

percentages of RPS (for the psychotherapy group) and RDS (for the biological psychiatry group), derived from the results of the logistic transformations, the differences from the observed data were not statistically significant ($\chi^2 = 5{\cdot}97$, and 11·02, respectively, both with d.f. = 6).

Therefore, to achieve the aim stated above, a logistic transformation and multiple regression analysis was then performed separately for each criterion group. The dependent variables were the logistic transformations of the cumulative percentages of (i) the psychotherapy group's scores on RPS (i.e., LOGIT-P), and (ii) the biological psychiatry group's scores on RDS (i.e., LOGIT-D). The predictor variables were the individual scores obtained from the respective 11 psychotherapy items or ten drug therapy items. The multiple regression equations for these relationships were: (i) for the psychotherapy criterion group, $\text{LOGIT-P} = 0.282(\text{RPS}) - 6.087$ ($R^2 = 0.954$; $F = 1459.\ 2$; d.f. = 1.70); and (ii) for the biological psychiatry group, $\text{LOGIT-D} = 0.277\ (\text{RDS}) - 7.320$ ($R^2 = 0.891$; $F = 827.7$; d.f. = 1,101).

The impact of these calculations is best illustrated by an example. If, for instance, a practitioner's RPS score was 25, applying the appropriate formula (i): $\text{LOGIT-P} = 0.282 \times 25 - 6.087$; and $\text{LOGIT-P} = 0.963$. From a table of logit transformations, the value 0·963 corresponds to a proportion of 72% and we can say that a RPS score of 25 or less was obtained by 72% of psychotherapists, or alternatively, that 28% of psychotherapists scored a RPS greater than 25. The procedure is analogous for RDS. Further scoring instructions and graphs which simplify the scoring technique are available from the authors.

Discussion

We have modified and shortened two scales for measuring practitioners' attitudes to psychotherapy and drug therapy. The resulting scales have been combined in a 21-item questionnaire, which is brief and easy to use, and should have wide application. The results of a concurrent validation of the scales, using two large and virtually unique criterion groups, consisting of consultant psychiatrists from the Royal College of Psychiatrists who were members of the Psychotherapy Section or the Biological Psychiatry Section, show the extent to which their attitudes to psychotherapy or drug therapy overlapped.

Clearly, the reliability and validity of the questionnaire depends to a large extent on the characteristics of the visual analogue scales we have used to measure the relevant attitudes to psychiatric treatment. Visual analogue scales have been used widely in psychiatry (Zealley & Aitken, 1969; Aitken 1969; Bond & Lader, 1974), and in a variety of medical and surgical contexts (Priestman & Baum, 1976; Downie *et al,* 1978; Maxwell, 1978; Blamey *et al,* 1984; Llewellyn-Thomas *et al,* 1984; Selby *et al,* 1984). In general, authors comment favourably on the reliability and validity of the method (Luria, 1975), though the assessment of these qualities has varied in degree. The main concerns are the reliability of such scales when they are re-scaled down to a smaller number of categories and the optimum number of such categories. Remington *et al* (1979) suggest that the question of reliability should not influence the choice of a categorical or continuous scale, or the number of scored points in the scale. McKelvie (1978) found that a continuous scale did not offer any advantages in terms of reliability or validity, though it was preferred by subjects; that a five-category scale was most reliable (on an attitude judgement task); and that there might be a loss of discrimative power and validity with fewer than five categories.

Attention has also been given to the place of data transformation in the analysis of information obtained from visual-analogue scales. In this respect, it is difficult to disagree with Maxwell (1978), who recommended that authors have valid reasons in their own settings for using such transformations.

Studies are now underway to develop the TAPS questionnaire further and, in particular, to determine its reliability and validity with different samples. Until these are completed, no information will be available on the reliability or predictive validity of the scales.

Appendix

The TAPS is constructed by re-ordering the following statements in the order indicated by the item numbers.

A) The 11 items which accounted for 90% of the variance in the psychotherapy score (PS)*

Item number	*Variable*	*Unstandardised regression coefficient*
7	Psychotherapy is more likely to be detrimental than beneficial	3.616
1	Enough is now known about psychotherapy to guarantee that we are on the right track	1.175
10	Research into the psychotherapeutic process has made monumental strides in the last decade	1.130
16	Psychotherapy is the treatment of choice in all psychiatric disorders	2.067
3	The grounds upon which the edifice of psychotherapy rests are at least 50% the fantasy of its creators	1.140
17	The purported cures achieved through psychotherapy really tell us more about the therapist than about the patient	1.261
13	That psychotherapy is considered an effective means of curing mental illness is evidence of the power of a mass delusion	1.365
5	A well controlled study of the results of psychotherapy over a five-year period is needed	0.815
6	Psychotherapy is neither as valuable as its adherents claim nor as dangerous as its opponents believe it to be	0.906
12	Psychotherapy is an unknown quantity among medical treatment methods	0.935
18	Psychotherapy is the only treatment of emotional problems which offers any hope of success	0.783
	Constant	4.046

B) The ten variables which accounted for 91% of the variance in the drug therapy score (DS)*

Item Number	*Variable*	*Unstandardised regression coefficient*
8	Psychotropic drugs have their place in psychiatry	2.794
19	The use of psychotropic drugs has brought man's control of mental illness to a point similar to man's control of pain	1.578
20	Psychotropic drugs lead to miraculous recoveries in mentally ill persons	1.507
15	The use of psychotropic drugs offers very little to psychiatric treatment while presenting many risks, problems and obstacles to more effective treatment	2.090
4	The use of psychotropic drugs has facilitated the management of the hospitalised mentally ill and aids in creating a state more favourable for psychotherapy	1.572
2	Psychotropic drugs are being used too frequently and with little thought to the individual patient	0.993
11	Use of psychotropic drugs may or may not be helpful to patients with emotional illness	1.122
9	Psychotropic drugs constitute a major breakthrough in our attempts to help the mentally ill	1.257
14	Psychotropic drugs cure nothing and can often confuse the treatment	1.481
21	The use of psychotropic drugs should be definitely discouraged in psychiatric treatment because of their doubtful value and the danger to the patient	2.206
	Constant	3.950

Method of scoring: The visual analogue scale data were re-scaled into five categories (scores 0–20=2; 21–40=1; 41–60=0; 61–80=−1; and 81–100=−2; or *vice versa*). Item numbers 2, 3, 4, 6, 8, 10, 14, 15, 17, 18, 20, 22, 23, 26, 27, 28, 29, 30, 35, 37, and 40 were scored in the manner illustrated, and the remaining items were scored in the opposite way. To obtain the revised psychotherapy score

(RPS), the re-scaled values for the psychotherapy items were each multiplied by the appropriate unstandardised regression coefficient, the resultant values were summed, and the constant was added. An analogous procedure was used to calculate the revised drug therapy score (RDS).

The proportion of psychotherapists achieving a given RPS score can then be obtained from the multiple regression equation provided i.e., $\text{LOGIT-P} = 0.282\,(\text{RPS}) - 6.087$. The procedure with RDS is analogous to this.

*The statements in each list are listed in rank order of their contribution to the variance.

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*Greg Wilkinson, BSc, MPhil, MBChB, MRCP, MRCPsych, *Honorary Lecturer and Honorary Senior Registrar.*
Paul Williams, MB BCh, MRCPsych, *Senior Lecturer and Deputy Director.*

General Practice Research Unit, Institute of Psychiatry, De Crespigny Park, London SE5 8AF

*Correspondence

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Comment

Positive and Negative Symptoms in Psychiatry

MICHAEL R. TRIMBLE

The terms positive and negative symptoms have slipped into the language of contemporary psychiatry with comparative ease. It is not uncommon for these expressions to be used with little explanation, both at meetings and in written communications, with the implicit understanding that their meaning is understood and that somehow they are of value to our knowledge of psychopathology. However, that there are no clear guide-lines at present for our use of these terms is shown from a recent survey of psychiatrists' opinions from a market research company (Martin Hamblin Research-Personal Communication). As part of a series of questions asked to many psychiatrists of differing age, geographical location, and status, they were asked about the meaning of these terms, positive and negative symptoms and the proportion of schizophrenic patients having them. Of the categories quoted by Crow (1980:81) as positive symptoms, 68% considered that delusions were positive symptoms, 63% hallucinations, and only 35% thought disorder. In contrast, 18% thought that behaviour disturbance was a positive symptom, a similar figure (15%) being given for passivity feelings. Considerable variation was noted, however, with hallucinations being considered positive by only 33% of London psychiatrists, thought disorder by only 11% of those qualified 16–25 years, and one-quarter of all registrars and psychiatrists from Midland Health Districts considered passivity feelings to fall into this category. Even greater disagreement was recorded for negative symptoms. Thus, the symptom most often associated with this category was apathy, by 52% of respondents. Only 26% considered that withdrawal was a negative symptom, the percentage data for lack of motivation and blunting of affect being 37% and 15% respectively.

Although credit for the introduction of these terms is usually given to Hughlings Jackson, it has recently been suggested that the distinction should be attributed to John Russell Reynolds (Berrios, 1985). In any case, it is clear from the writings of Hughlings Jackson that he expressed his own debt to predecessors with regard to the development of his own ideas. Amongst those quoted are Dr Thomas Laycock, Dr Dickson Thompson, Dr Anstie, and Dr Henry Munro.

Jackson elaborated a scheme of nervous function based in part on his extensive and first-hand knowledge of epilepsy. The main elements of this were his emphasis on a physiological approach and four basic ideas. The latter were the evolution of nervous functions, the hierarchy of functions, the principal of dissolution, either local or uniform, and the negative and positive symptoms that arise from dissolution (Ey, 1978). The concept of positive and negative symptoms is clearly outlined in several of his papers; "The negative element in the symptomatology is what the epileptic discharge produces; it is the dissolution.... the positive element is physical activity of the lower nervous arrangements, which are, except for overactivity, healthy". (Jackson 1881). In this scheme, therefore, the positive elements are seen as resulting, not directly from any disease process, but from the integrated action of the rest of the functioning nervous system. Implicit in these ideas are that positive and negative symptoms are closely intertwined such that they both occur contemporaneously, the pathology that gives the negative symptoms at the same time allowing expression of the positive symptoms. In contrast to this, the concept which derives from Reynold's view allows the positive and negative symptoms to be independent, since negative symptoms are seen to relate to loss of "vital properties" of nervous arrangements, while positive ones derive from an excess of such properties (Reynolds 1861). For both authors, however, symptoms were related to some underlying mechanism of CNS function.

Jackson specifically considered mental disorders and their genesis. He suggested that in all cases of insanity, the principal of dissolution, the level of evolution that is remaining, and the positive and negative elements need to be considered. Further, the consequences were dependent upon other factors, which included the depth of the dissolution, its general or partial nature, the person undergoing the dissolution, the rate at which the dissolution was effected, and the influence of external circumstances (Jackson 1884). Here was a general model for the symptoms of nervous diseases, which included application to psychiatric diseases, in marked contrast with the limited way in which positive and negative symptoms are employed today, mainly or almost exclusively being used in the context of schizophrenia.

Of course, since Jackson was writing, our ideas of the way the brain may function have changed considerably. In particular for psychiatry, the development of the concept of the limbic system (Papez, 1937; MacLean, 1970) has allowed us a more secure footing for the foundation of a renewed understanding of mental disease, with the brain in mind. Thus, many psychiatric conditions may be considered to reflect, in part at least, disturbed limbic system function, schizophrenia being a clear example. As pointed out above, there seems little agreement amongst psychiatrists at the present time as to the meanings of the term positive and negative, one reason for this being that their current use appears to be purely descriptive, and devoid of any attempt to introduce *mechanism*, which was the intention of both Reynolds and Hughlings Jackson. There is, however, a sub-set of positive symptoms about which there is more agreement with regard to definition, namely the first-rank symptoms of Schneider. These have assumed considerable importance in British Psychiatry since their delineation in 1939, especially in view of Schneider's claim that a first rank symptom "always signifies schizophrenia" (Schneider, 1957). However, their pathognomonic basis has been questioned by several authors (Silverstein & Harrow, 1978; Radhakrishnan *et al*, 1983) and their definition has been shown not to be as straight forward as it first appears (Koehler, 1979). There is nevertheless the suggestion that first-rank symptoms may relate to a poorer outcome (Silverstein & Harrow, 1978), to a poor response to ECT (Koehler & Sauer, 1983), and in genetic studies show no hereditability (McGuffin *et al*, 1984). Thus, although first-rank symptoms appear to be more readily identifiable and more clearly defined than the loose descriptive terms positive and negative symptoms, their status as important clinical markers in psychiatry seems to be declining. It is of interest therefore that their presence in another disorder, namely temporal lobe epilepsy, the epileptic condition that so interested Jackson, may be providing us with important evidence regarding their pathogenesis.

Thus, the relationship between epilepsy and psychosis has been recognised for many years, although the extensive study of Slater & Beard (1963) emphasised in particular the presence of first-rank symptoms in their sample, a large percentage of which has temporal lobe epilepsy. Several authors recently have attempted more precisely to define the presenting phenomenology of patients with psychosis and epilepsy, in particular, comparing this to patients with process schizophrenia, using such techniques as the Present State Examination (Perez & Trimble, 1980; Trimble & Perez, 1982; Perez *et al*, 1985). In these studies, patients categorised as having nuclear schizophrenia (NS) by the CATEGO programme, were exclusively drawn from patients with temporal lobe epilepsy having complex partial seizures, with or without secondary generalisation. Further, they were more likely to have this presentation if the epileptic focus was lateralised to the dominant hemisphere. These data, in particular the laterality data, support the findings of others (for review see Trimble, 1984) namely that in patients with temporal lobe epilepsy and psychosis, the latter is likely to be schizophreniform when the dominant hemisphere is principally affected.

Aside from epilepsy, also in the literature is growing evidence of a bias towards left-sided brain dysfunction in schizophrenia (Gruzelier & Flor-Henry 1979; Flor-Henry & Gruzelier 1983). In some of these studies, a specific link to first-rank symptoms has again been recorded, for example in the paper of Connolly *et al* (1983), who showed in evoked potential studies that an increasing amplitude-intensity pattern for the P100 peak at the left temporal location was seen in schizophrenic patients with higher scores for NS on the PSE.

One interpretation of these data, which has relevance for the issue of positive and negative symptoms, is that certain positive symptoms (the first-rank symptoms of Schneider) signify for the observer dysfunction in the dominant hemisphere, especially in the temporal-limbic areas. This suggestion is no more or no less than a similar statement that may be made about the site of lesions in an aphasic patient, although the suggestion that speech mechanisms could be related to brain laterality was not accepted until many years after the association was discussed and recorded by Broca. Abnormalities in this crucial area, as found in the temporal lobe epilepsy model of schizophrenic symptoms, may thus lead to negative symptoms, in the Jacksonian sense, of memory and possible other cognitive impairments, and, on account of the continued functioning of the surrounding cortical areas, a variety of disturbances of sensory information, especially auditory hallucinations, and thought disorder of a rather specific type. Why there should be this specificity, at the present state of our knowledge is unknown, be it similar to the apparent specificity of aphasic syndromes dependent upon the region of the dominant hemisphere that is damaged (Benson 1979).

To attempt an understanding of positive and negative symptoms in relationship to brain dysfunction, as was Jackson's approach, would seem to be more appropriate than the purely descriptive approach being developed in psychiatry at the present time. This will attempt to support a nosology about which there will be no agreement, and shift the long-standing disagreements, which have done so much harm to the discipline from 'what is schizophrenia', to 'what are positive and negative symptoms'. Similarly, the possible subtle links between positive and negative symptoms will be missed if they are purely ascribed to an increase or decrease of various transmitters in selected regions of the brain, with little reference to the surrounding structures or knowledge of cognitive neuropsychiatry. It is implied, therefore, that, while both Hughlings Jackson and Reynolds may have discussed the terms positive and negative with regard to symptoms of nervous disease, it is the line of Jackson that today we should be following, and to ignore completely historical etymology is not only improper but will merely serve to obfuscate.

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Michael R. Trimble, MRCP, FRSPsych. *Consultant Physician in Psychological Medicine and Senior Lecturer in Behavioural Neurology, The National Hospitals for Nervous Diseases, Queen Square, London WC1N 3BG.*

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Comparative Effects of Seven Antidepressant Regimes on Appetite, Weight and Carbohydrate Preference

Appetite, weight, and preference for carbohydrate-containing food were followed in patients treated in double-blind trials of seven antidepressant regimes. Trimipramine and isocarboxazid combined had a significant effect in increasing appetite, carbohydrate preference, and weight; in patients who had lost appetite at presentation and were on this treatment, improvement in Hamilton score was linked to increase in weight – a finding not true of the other treatments.

Appetite and weight change have often been used to assess both the severity and nature of depression, e.g. both the Hamilton and Beck rating scales use appetite and weight loss as features of 'endogenous' depression.

It is also known that antidepressants have an effect on appetite and weight, and in the long term, can be associated with disproportionate appetite and weight gain (Paykel *et al* 1973), but little information is available concerning the comparative effect of various antidepressant regimes. This information would be of use for a number of reasons: e.g. in choosing a regime where increase in appetite and weight are particularly necessary, or on the other hand, in avoiding such a regime where there are already problems of over-weight.

In addition to drug treatment, appetite history and weight history are important factors, associated with appetite and weight change, both in the development and treatment of a depressive illness (Crisp *et al* 1976; Harris *et al* 1984). Results are reported here on the comparative effects of seven antidepressant regimes in 168 moderately depressed outpatients, who had presented with a spectrum of depressive disorder.

Method

Depressed outpatients ($n = 168$) with Hamilton scores ranging from 12–50 (corrected for appetite and weight loss) had fulfilled Feighner's criteria for a primary depressive illness. They were involved in two double-blind antidepressant trials, in which they completed a six-week course of one of the following oral antidepressant regimes: Flupenthixol or amitriptyline, and trimipramine, phenelzine, isocarboxazid, trimipramine and isocarboxazid in combination, and trimipramine and phenelzine in combination. The only other medication allowed was diazepam, 5 mgs tds (optional) and nitrazepam at night.

A flexible dosage schedule was used, the dose being adjusted according to the clinical state or side-effects of both. Mean dosages (in milligrams) during the last three weeks of trials were: phenelzine (45), isocarboxazid (32), phenelzine + trimipramine (44 + 102), isocarboxazid + trimipramine (30 + 96), amitriptyline (125), flupenthixol (2.5), trimipramine (106).

None of the patients had been on antidepressant medication in the three weeks prior to presentation, although many had been in the past. Together with a battery of questionnaires, each patient was assessed for appetite at presentation and at six weeks.

Assessment of appetite and carbohydrate craving

Appetite was assessed on each occasion using a visual analogue scale which had been marked into 14 increments; seven was the mid-point of the scale and represented the patient's appetite when completely well. Either side of the point represented increase or decrease in appetite, and it was carefully explained to the patient that the increments were: minimal, mild, moderate, severe, or extreme, in both directions. Preference for carbohydrate-containing food was also measured on each occasion, but only an increase was noted (from normal to mild, moderate, or severe). These methods of assessment are useful for showing changes in appetite and carbohydrate preference over a period of time as a response to treatment.

Among the 168 patients, 90 presented with a history of decreased appetite; in the remaining 78, appetite was assessed as either equal to or greater than normal. These two sub-groups were analysed separately.

Weight

The patient was weighed on the same scales throughout the study, wearing similar clothes.

Results

The treatment trimipramine plus isocarboxazid in combination was associated with the greatest increases in

TABLE I

Change in appetite, weight and carbohydrate preference among 90 subjects who had lost appetite at presentation by drug regime
(i.e. after 6 weeks treatment)

		Appetite change		*% Weight change*		*CHO preference change*		*Hamilton Score change*	
Drug regime	n.	mean	(sd)	mean	(sd)	mean	(sd)	mean	(sd)
Trimipramine	17	+1.9	(2.2)	+3.3	(2.4)	+0.6	(0.7)	−11.6	(8.8)
Phenelzine	11	+2.2	(2.5)	+1.0	(6.2)	+0.4	(0.9)	−11.4	(10.8)
Isocarboxazid	10	+3.0	(2.2)	+2.8	(4.9)	+1.0	(1.3)	−13.5	(6.2)
Trimipramine + Phenelzine	13	+2.7	(2.5)	+3.9	(2.3)	+0.9	(1.3)	− 8.8	(10.3)
Trimipramine + Isocarboxazid	13	+4.0	(3.9)	+8.2	(6.9)	+1.7	(1.4)	− 7.4	(10.9)
Amitriptyline	14	+2.7	(2.2)	+3.0	(2.4)	+0.6	(1.1)	−10.2	(7.6)
Flupenthixol	12	+2.1	(2.5)	+1.6	(3.5)	+0.3	(0.9)	− 7.1	(8.9)
All who had lost appetite	90	+2.6	(2.6)	+3.5	(4.7)	+0.5	(1.2)	− 9.9	(9.2)

appetite, weight, and carbohydrate preference, both in the population as a whole and in the 90 patients presenting with appetite loss. The Table shows changes in these three variables and in Hamilton scores, according to appetite at presentation, and whether this particular treatment combination was used.

Flupenthixol, the only antidepressant with a presumably radically different mode of action (i.e. dopamine antagonism) did not differ from other treatments in its effect on appetite, carbohydrate craving, and weight.

Analysis of variance showed that among the 90 subjects who had presented with appetite loss, the treatment combination of trimipramine and isocarboxazid differed significantly from the other six regimes put together in its effect on weight ($P<0.001$), carbohydrate preference ($P<0.01$), and appetite ($P<0.05$). The increase in these parameters on the other six regimes were very similar to one another (Table). There were no significant differences in the changes in Hamilton scores between groups. However, in those 13 patients with initial low appetites, who received trimipramine and isocarboxazid in combination, there was a striking tendency for affective improvement in Hamilton score to be accompanied by weight gain. The correlation of -0.86 is highly significant (2 tailed $P<0.00041$). It seems, therefore, that if a patient initially has a depressed appetite, and is treated with trimipramine and isocarboxazid, a considerable weight gain is likely to occur, particularly when the patient shows a concomitant reduction in clinical depression. This is illustrated in the scattergram (Fig. 1).

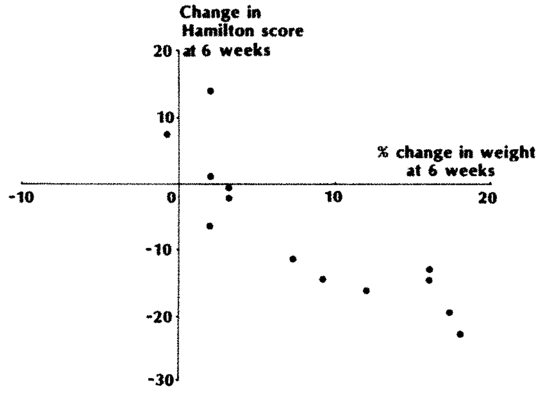

FIG. 1 Scatter diagram of change in Hamilton score by change in weight for 13 patients on isocarboxazid and trimipramine in combination, and who presented with loss of appetite.

No difference between drug regimes were evident among the 78 patients without appetite loss; in these, and in all treatment groups other than combined trimipramine and isocarboxazid, no such relationship as that shown in Figure 1 was found.

Discussion

The results of the study in terms of antidepressant activity showed no major significant differences for different antidepressant regimes (Young *et al*, 1976, 1979). The changes in appetite, carbohydrate craving, and weight for the population as a whole have shown that in mild to moderate depression, the important associations are with previous appetite and weight history, and that what has happened at presentation is reversed to some extent after six weeks' treatment (Harris *et al*, 1984a).

Bearing these two findings in mind, it is not surprising that there is little difference between drug treatment groups in terms of effect on appetite, carbohydrate craving, and weight. In other words, what is true for the population as a whole is true for six of the treatment sub-groups, but the exception is the group on trimipramine and isocarboxazid in combination, in which increase in appetite carbohydrate preference, and weight are significantly greater. Although not associated with greater antidepressant activity (despite the increased dosage of antidepressant in comparison with other groups), there is a marked association of increase in appetite and weight with antidepressant activity within the group itself. Why this should be so is unknown, but the finding is only true for those patients who were on this combination and whose appetite was decreased at presentation. It does not extend to the group on this drug combination whose appetite had remained the same or had increased at presentation. The finding therefore demonstrates an interaction between loss of appetite and the pharmacological action of the combination. Secondly, in the original design of the antidepressant trials, two mono-amine oxidase inhibitors were chosen, one a weak inhibitor (isocarboxazid), and the other a strong inhibitor (phenelzine). If the effect on appetite were related to the MAOI component of combined treatment, then it would be expected to be present even more so with the combination trimipramine and phenelzine. However, this is not the case. The effect is worthy of note, since this combination may be of particular use where weight increase is desirable.

We have shown that increases in appetite, weight, and carbohydrate craving are important components of recovery in the particular circumstance where they are decreased at presentation and where this particular pharmacological combination is used. It is not possible to explain why, in the light of current knowledge, but numerous neurotransmitters are known to be involved in feeding behaviour, including endorphins. (Cooper *et al*, 1984), 5 H.T., nor-adrenaline, and dopamine.

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*Brian Harris, BSc, MB, BS, MRCPsych, *Consultant Psychiatrist and Honorary Lecturer, Department of Psychological Medicine, University of Wales College of Medicine, Cardiff.*

John Young, MD, MPhil, *Consultant Psychiatrist, Department of Psychological Medicine, St. Thomas' Hospital, London, SW1.*

Bill Hughes, MB, BS, MRCPsych, *Consultant Psychiatrist, David Rice Hospital, Norwich.*

Statistics were carried out by Robert Newcombe, PhD *Department of Medical Statistics, University of Wales College of Medicine, Heath Park, Cardiff.*

*Correspondence

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Schneiderian First-Rank Symptoms Caused by Benzodiazepine Withdrawal

Benzodiazepine withdrawal has been found to give rise to numerous physical and psychological symptoms. This paper describes, for the first time, Schneiderian first-rank symptoms of schizophrenia caused by such withdrawal.

Kurt Schneider first introduced the concept of 'first-rank symptoms' of schizophrenia in 1939, and these became more widely known when his original book was translated into English in 1959. Despite being found in only 72% of schizophrenics (Mellor 1970), their use as operational criteria for the diagnosis of schizophrenia has become worldwide. So much so that patients experiencing them are sometimes erroneously diagnosed as being schizophrenic, despite the presence of an organic or toxic pathology. We present the histories of two patients who experienced first-rank symptoms brought about by benzodiazepine withdrawal – a phenomenon not previously described.

Case 1

The patient was a 51 year-old lady, who had been treated by her general practitioners for depression for over 12 years, receiving various benzodiazepines, most commonly chlordiazepoxide combined with amitriptyline, as Limbitrol-10, using 4–5 tablets daily.

After slightly reducing her alcohol intake and suddenly stopping her benzodiazepines, she was admitted to a psychiatric hospital expressing paranoid ideas. She was diagnosed as suffering from delirium tremens, and treated with chlorpromazine and vitamin injections.

She discharged herself against medical advice and returned home, where she became increasingly paranoid about her neighbours. She experienced auditory hallucinations in the third person ('There she goes again') and thought broadcasting, believing her neighbours knew her thoughts as they happened. On the day of her first suicide attempt, several weeks later, she heard voices which she interpreted as wishing to kill her, and stabbed herself in the neck, puncturing her oesophagus and trachea. She was admitted to hospital, where her injuries were successfully repaired.

She was initially treated with diazepam, 10 mg on a once-daily prn basis, though this was stopped after three days. She was diagnosed as suffering from a paranoid psychosis and trifluoperazine, 5 mg tds was started 12 days after admission, but with little effect.

Sixteen days after admission, she received diazepam, 5 mg tds, until her transfer and first admission to the catchment area psychiatric hospital. According to the patient, the diazepam had made the hallucinations disappear. The diazepam was then stopped and she was treated with trifluoperazine alone, but her condition deteriorated, and she experienced further auditory hallucinations. After five days, her case was reviewed and a diagnosis of benzodiazepine withdrawal was made. She was started on diazepam, 5 mg qds, which abolished the hallucinations on the first day of treatment. She was placed on a withdrawal regime, with no subsequent recurrence of psychotic symptoms.

She took her own discharge one month after transfer, but was followed-up by a community psychiatric nurse on three occasions, at which times she was symptom-free. However, within a week, because of difficulties in a sexual relationship, she restarted Limbitrol and alcohol. She was advised not to take the tablets, and was encouraged to attend the out-patient clinic; 18 days after discharge, the day before her out-patient appointment, she drank bleach, poured a flammable liquid over herself and set fire to it, dying 36 hours later from 44% burns.

In view of her previous suicide attempts, it was concluded that the withdrawal psychosis had returned, reproducing the suicidal ideation, after self-initiated sudden withdrawal from benzodiazepines.

Case 2

The patient was a 40 year-old woman with a 14-year history of benzodiazepine usage. Her prescribed medication was diazepam, 5 mg tds, but she readily admitted to often taking three times this dose, the extra being bought illegally.

She showed no psychiatric symptoms until 1970, when she was started on diazepam for anxiety following a miscarriage. Since 1973, she had had many admissions to psychiatric hospital, being diagnosed as suffering from a personality disorder and depressive episodes.

She was again admitted in 1984, after her boyfriend had left her, because she was behaving in a bizarre manner and taking up odd postures. Although full assessment of the mental state was impossible, as she was withdrawn and only communicated in nods, she gave no indication that she was responding to hallucinations or to passivity feelings.

She was initially treated with chlorpromazine, 100 mgs tds, procyclidine 5 mgs tds, and amitriptyline, 100 mgs nocte, and her diazepam tablets were stopped. After five days, she started to complain of hearing voices, but was unable to understand what was said, as they spoke too quickly. After a further five days, because of the minimal improvement in her condition, the dose of chlorpromazine was increased by 200 mgs nocte. Two and a half weeks after admission, she claimed that voices told her to 'go to hell'. Sulpiride, 200 mgs twice a day was started, and later her amitriptyline was increased to 150 mgs nocte.

Later, she had a violent outburst in response to voices which were discussing her in the third person, and complained that certain television programmes upset her. It was also noted that she was experiencing thought blocking. The dose of sulpiride was increased to 400 mgs twice a day, though this was later stopped after having negligible effect.

Further aggressive outbursts occurred, which responded very well to injections of sodium amytal, and she was therefore started on a reducing dose of chlormethiazole, on which she rapidly settled. Her improvement was such that she was discharged seven weeks after admission.

Discussion

The above patients both showed Schneiderian first-rank symptoms after cessation of benzodiazepine use: in the first case, hallucinations discussing the patient in the third person and thought broadcasting; in the second case, hallucinations discussing the patient in the third person. In addition, both experienced feelings of intense paranoia, and their behaviour was at times quite disturbed. These factors could have been made the basis for a diagnosis of acute schizophrenia if the cessation of benzodiazepines had not been noted.

These cases highlight the possible psychological withdrawal symptoms of benzodiazepines and should be borne in mind when prescribing or contemplating ceasing the prescription of this group of drugs. It was first demonstrated by Hollister in 1961 that sudden reduction of benzodiazepines could cause withdrawal symptoms. More recently, there has been evidence to show that even in therapeutic doses, benzodiazepines can cause dependence manifest mainly by withdrawal symptoms (Pevnick *et al* 1978; Winokur *et al*, 1980; Petursson & Lader, 1981; Tyrer *et al*, 1981, 1983; Ashton, 1984). There has been a tendency to highlight the physical aspects of benzodiazepine withdrawal, particularly headache, muscular pain, tremor, ataxia, paraesthesia, abdominal pain, nausea, vomiting, diarrhoea or constipation, and weight loss. However, psychological symptoms are also very common, including anxiety, agitation, irritability, impaired memory and concentration, insomnia, depersonalisation and derealisation, paranoia and hallucinations. (Preskorn & Denner, 1977; Fruensgaard, 1976; Petursson & Lader, 1981; Ashton, 1984).

The two patients described above are the first to be reported as suffering from Schneiderian first-rank syndrome, highlighting the dangers of prolonged treatment and subsequent withdrawal from these drugs.

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*Keith Roberts, MB, ChB, MMedSc, MRCPsych, *Senior Registrar, Dept. of Psychological Medicine, St. Thomas' Hospital, London SE1 7EH.*

Neil Vass, MB, BS, DRCOG, *GP Trainee, St. Thomas' Hospital, London SE1 7EH.*

*Correspondence

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Manic-Depressive Psychosis in a Mentally Handicapped Person: Diagnosis and Management

The diagnosis of manic-depressive psychosis in mentally handicapped people can be easily overlooked, partly because its presentation differs from that in people with normal intelligence. This report illustrates some of the difficulties involved in making the diagnosis of manic-depressive psychosis in a mentally handicapped person and in planning for her future care.

The coexistence of mental illness and mental handicap poses a considerable diagnostic challenge. Nevertheless, identification and management of any existing psychiatric disorder is important, because such disorders compound difficulties in adjustment and put extra pressure on the carers. Until recently, some writers considered exclusion of mental handicap as a prerequisite for the diagnosis of mental illness (Schneider, 1959; Winokur, 1974). It has been established now that mentally handicapped people have an increased vulnerability to psychotic disturbances (Eaton & Menolascino, 1982). However, the diagnosis of manic-depressive psychosis in a mentally handicapped person is a difficult one and can be easily missed.

Pollock (1945) examined the psychiatric diagnoses of 444 mentally handicapped people admitted for the first time to New York State Hospital between July 1941 and June 1942, and found seven cases (1.6%) of manic-depressive psychosis. Reid (1972) found that the incidence of manic-depressive psychosis in a hospitalised population of mentally handicapped people was 4.4%. Heaton-Ward (1977) reviewed the case notes of 484 mentally handicapped hospitalised patients; ten (2%) were given the diagnosis of manic-depressive psychosis.

Once the diagnosis of manic-depressive psychosis is established, treatment with lithium may prove to be helpful. Naylor *et al* (1974) showed significant reduction in the duration of illness in a two-year double-blind crossover study, using lithium to treat 14 mentally handicapped people with manic-depressive psychosis. Rivinus & Harmatz (1979), in a single-blind placebo controlled study, showed significant improvement in all the symptoms of affective disorder and also a reduction in the number of relapses. Phenothiazines and butyrophenones are amongst other suggested treatments.

This paper reports a case of manic-depressive psychosis which presented over the years as schizophrenia, and which has responded to treatment with lithium carbonate.

Case Report

AC is now in her early sixties. She has lived in a psychiatric hospital for the past 13 years. She went to the same school as her brother and sister, but stayed one year longer because she was found to be 'backward'. Her birth and childhood were otherwise normal.

After leaving school at the age of 15, she started work in a local factory. At 18, she found it difficult to cope with the job, and complained that the men at work were teasing her. At the same time, there were air raids, which upset her. She was admitted to a psychiatric hospital in an excitable, noisy state. There, she was found to be manneristic, laughing, emotional, and crying. A diagnosis of schizophrenia was made and she was treated with insulin and ECT. She was noted to be moderately mentally handicapped. She stayed in hospital for two years; a year after discharge, she was readmitted with a history of weight loss and poor sleep. This admission may have been precipitated by the death of an old friend; she stayed for a year, again recovering with insulin therapy and ECT. She was described as a clean, tidy person with a shy and sensitive personality.

When AC was 48, her father was admitted to hospital for a significant physical illness. Her mother had died some 4 years earlier, and she was unable to support herself alone. By this time, she had more than 12 admissions to psychiatric hospitals and had spent nearly 15 years as an in-patient. Between admissions, she had lived happily with her parents, attending an adult training centre and regularly visiting a psychiatric out-patient clinic.

Admission was then arranged in a mental handicap hospital on a permanent basis. She initially appeared to settle, but about two years after admission, she became excitable, restless, and hostile, laughing incessantly, talking to herself and to God with marked pressure of speech. She became disinhibited, wandered naked, demanded attention, and smoked heavily. She also neglected herself, lost weight, slept poorly, and was incontinent. This behaviour lasted for several months, followed by a period of two weeks, when she was quiet and able to take care of herself. Staff commented at this time that she was pleasant and likeable. Episodes of such disturbed behaviour recurred during the following twelve years. On some occasions, she was transferred briefly to a psychiatric hospital, where she received ECT without lasting improvement. Large doses of phenothiazines and butyrophenones were given; she was also put on benperidol for her disinhibited behaviour, but she continued to be difficult to manage.

Her history and mental state were then reviewed. The cyclical nature of the heightened mood in the setting of a well preserved personality and a relatively good premorbid adjustment were suggestive of manic-depressive psychosis, and this diagnosis was further supported by the positive family history—in the past, her mother had been admitted to a psychiatric hospital with affective disorder.

On 600 mg of lithium per day, she attained therapeutic plasma lithium levels, her mood stabilised, she became co-operative, pleasant, amenable, involved in ward and occupational therapy activities. Considerable improvement in sleep, appetite, and concentration was noted. Her relationships with others, her communication skills, and personal hygiene improved remarkably; she gained in self-esteem and her smoking was reduced. She began to be liked by both staff and other residents. For the first time since admission, her sister requested permission to take her home for a weekend. Both her sister and brother-in-law noticed the change in her, and enjoyed the three days of companionship.

Ten months later, she remained on lithium and had only one mild manic episode which lasted for 2 to 3 weeks, brought under control by adding thioridazine, 25 mg b.d. to the treatment regime. It is anticipated that A C will continue to take lithium for at least two years, under the care of a psychiatrist with an interest in mental handicap.

Discussion

It has been demonstrated that among the non-mentally handicapped population, many individuals subsequently diagnosed as suffering from mania have previously been thought to have schizophrenia (Carlson & Goodwin, 1973; Taylor & Abrams, 1973; Tyrer & Shopsin, 1982). This misdiagnosis may be more common in mental handicap, due to under-reporting of depressive or manic symptoms by carers (Hasan & Mooney, 1979).

In retrospect, AC exhibited several symptoms of mania on her first and subsequent admissions, but her elation was poorly sustained and lacked an infectious quality. Hallucinations and delusions were simple and naive, lacking wit and humour, in keeping with Reid's (1972) observations on mentally handicapped people with mania. It seems likely that her limited vocabulary and intellectual level were modifying the presentation of her psychopathology.

She may be discharged to community facilities, but if community-based mental handicap services are to be successful and to function efficiently, then early identification and efficient treatment of psychiatric disorders are vital; this is clearly the role of the psychiatrist (Bicknell, 1985; Heaton-Ward, 1977). Better training for nurses in the fields of clinical psychiatry and psychopharmacology and encouragement for psychiatrists to maintain their diagnostic and treatment skills are essential in the interests of better mental health for mentally handicapped people.

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S. R. Kadambari, MB, BS, MRCPsych, *Senior Registrar in Psychiatry of Mental Handicap, Guy's Hospital, St. Thomas Street, London SE1 9RL.*

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Does Viloxazine Really Improve Sex Drive? A Double-Blind Controlled Study

The action of viloxazine on libido and sex drive was evaluated with a randomised controlled double-blind trial against placebo on a population of 26 male out-patients affected by primary depression (DSM III). Modifications in the sexual sphere were assessed by the ad hoc inclusion of a series of items in the Zung Self-Rating Depression Scale. Thus modified, the scale was administered at the beginning and the end of a four-week trial period. Viloxazine proved to have a considerable disinhibiting effect, whose principal expression level was a return to pre-depression levels of frequency in sexual relations.

Disorders of sexual function are frequently observed in the course of depressive diseases (De Leo & Magni, 1983). The antidepressants now available are generally efficacious in the treatment of these sexual symptoms, as well as of the other somatic ones, but it has been shown that these drugs may themselves sometimes be responsible for the onset of alterations in libido and in sexual drive (De Leo & Magni, 1983). These iatrogenic phenomena may constitute a serious hindrance to recovery from the depressive episode, especially when their importance is underestimated by the doctor, or when the patient does not reveal their onset.

Almost all the commercially available antidepressants have been associated with the development of sexual side-effects; however, viloxazine – an atypical antidepressant (Pinder *et al*, 1977) – showed a stimulating effect on the sexual sphere in a previous open trial (De Leo *et al*, 1983). In fact, it produced significantly greater improvements in sexual symptoms than it did in other features of depression. The present study investigates the effect of this drug on sexual function with a randomised double-blind trial against placebo in patients suffering from primary depression (DSM III).

Method

Twenty-six male out-patients, age-range 29 to 62 years, were included; 24 were married, and two separated but cohabiting with new partners. All were diagnosed as having primary depression and included: ten cases of major depression (four in their first episode); two of bipolar depressive disorder, and 14 dysthymic disorder. All were motivated for out-patient treatment with psychotropic drugs, and all observed a period of wash-out (except from benzodiazepines) lasting seven days. Patients with schizophrenia, drug abuse, alcoholism, cerebral lesions, convulsions, or major organic diseases were excluded. All subjects defined their sex-life during euthymic periods as satisfying.

Viloxazine and placebo were randomly assigned for a period of four weeks: during the first, the subjects took two tablets (200 mg of the drug), while a third tablet was added at the beginning of the second week. A benzodiazepine drug – lorazepam (max. daily dose 7.5 mg) or oxazepam (max. daily dose 90 mg) – was added in all cases. Depressive symptoms were evaluated at the beginning and end of the trial with the Zung Self-Rating Depression Scale (SDS) (Zung, 1965), with the modifications described elsewhere (Magni *et al*, 1981). Four additional items were included in the SDS: 'I have trouble achieving erection; Since I've been feeling down, my sexual activities have fallen off; It seems to take me longer than usual to achieve climax; Ejaculation is difficult or takes longer.' This expanded version of the Zung scale was tested on a group of 60 psychiatric patients, 40 surgical patients, and 40 healthy subjects, all in an age-range of 20–65 years. The internal consistency of the modified SDS, measured with alpha coefficient, proved to be almost identical to that of the original SDS (0.86 vs 0.87). The new items showed high stability on test-retest, with correlations varying between 0.85 and 0.92 and retest times ranging from one week (surgical patients), through 15 days (psychiatric patients), to one month (psychiatric patients and normal subjects). Each patient was also submitted to a clinical global impression scale (CGI) before and after the trial.

Results

On opening the code, it was found that the viloxazine and placebo groups contained the same number of subjects (13 each); the mean ages of the two groups were respectively 46.42 (SD 11.29) and 48.66 (SD 10.15). There were two drop-outs, both cases of dysthymic disorders: the first, in the viloxazine group, complained of nausea and the second, in the placebo group, was injured in a road accident. The subjects treated with viloxazine spontaneously reported the following side-effects: nausea, loss of appetite, headache (1); nausea and loss of appetite (3); loss of appetite and heartburn (1); headache (1);

TABLE

Mean Scores at the SDS and at the Sex Drive (SD) Items

	viloxazine ($n = 12$)		*placebo* ($n = 12$)	
	SDS	*SD*	*SDS*	*SD*
1st evaluation	57.25	8.33	55.25	8.17
	(SD 8.34)	(SD 1.37)	(SD 6.59)	(SD 1.59)
	*T = 6.5	**T = 0	*T = 2	***T = 15
2nd evaluation	49.91	6.33	51.75	7.50
	(SD 5.76)	(SD 1.83)	(SD 6.69)	(SD 2.75)

Wilcoxon Matched-Pairs Signed-Ranks Test, two tailed: $*P < 0.01$; $**P < 0.001$; $***P$ N.S.

dizziness and dry mouth (1). The scores obtained on the SDS and on the items definable as sexual drive (SD) are shown in the Table.

There were no significant differences between the two groups in age, SDS scores, or SD scores, and no significant correlations in either group between age and SDS scores or age and SD scores, at either test or retest. The treatment with viloxazine gave rise to a significant improvement in depressive symptoms. The CGI confirmed improvements in eight of the subjects who received the drug (three very much improved, three moderately improved, and two slightly improved), while only four subjects in the placebo group had improved (three moderately and one slightly). The difference between the two groups was significant ($P = 0.005$, Fisher's Exact Probability Test). The most significant difference by the Wilcoxon test relates to the improvement in sex drive obtained with viloxazine. Separate examination of the individual items of the SD pool reveals a statistically significant difference for only one item in the viloxazine group. No. 10 ('Since I've been feeling down, my sexual activities have fallen off').

The SD scores at the beginning of the trial were approximately the same in both groups, and the greatest degree of impairment was this in item (10), with the same score in the two groups (3.00). One may therefore surmise that viloxazine acts on this level in particular, exerting an effect of disinhibition and favouring the recuperation of the subject's sexual activity. The fact that the answers to one item ('I still enjoy sex') did not undergo any significant modification during the trial may be considered to lend indirect support to the hypothesis formulated above: as libido remains more or less constant (the foregoing item evaluates libido), the intensification of sexual activity may rather be due to an effect of disinhibition exerted by the drug.

Comparing the scores on sexual items and those of the Zung scale as clustered by Blumenthal (1975) and then by Steuer *et al* (1980), there were, by the Wilcoxon test, significant improvements in the sex drive items ($P < 0.001$), total Zung scale ($P < 0.01$), depressed mood ($P < 0.05$), somatic symptoms ($P < 0.01$), and other somatic symptoms ($P < 0.02$). There was no difference between test and retest of all other clusters (well-being, optimism, and items not included in the clusters).

The responses to viloxazine also differed according to diagnostic categories; none of the scores for the five subjects with dysthmic disorders showed significant change at retest, while only the Optimism Index and the Depressed Mood Index did not change significantly in the major affective disorder group.

Discussion

Although differences in methodology and sampling prevent a direct summation of the findings of this trial with those of the previous one (De Leo *et al*, 1983), the present results partially confirm those obtained in open conditions. Our double-blind control provides further evidence for the ability of viloxazine to act specifically on sex drive; it seems to promote the recovery of sexual activity, probably by means of disinhibitory stimuli, more than by provoking a substantial increase in libido, or modifying other areas of sexual function. While the possibility that this particular sexual disinhibition might be non-specific cannot be completely excluded, as far as we are aware there have been no studies supporting the restoration of sexual activity as a consequence of treatment with antidepressants, without a contemporaneous restoration of libido.

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Diego De Leo, MD, *Clinical Assistant Professor**

Guido Magni, MD, *Clinical Assistant Professor, Universita degli Studi di Padova Istituto di Clinica Psichiatrica, 35128 Padova, Via Giustiniani 2, Italy.*

*Correspondence

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Grade Scores of the Montgomery–Åsberg Depression and the Clinical Anxiety Scales

Two recent observer rating scales for mood disorder are the Montgomery-Åsberg Depression Rating Scale, MADRS (Montgomery & Åsberg, 1979) and the Clinical Anxiety Scale, CAS (Snaith *et al*, 1982). These two scales have been developed from item analysis of longer instruments, and have the considerable advantage of brevity and therefore ease of administration. Unlike many scales, a further advantage is that both incorporate clear instruction about the allotment of grade scores on the individual items and both the scales avoid a major emphasis on somatic symptomatology, thus recommending their use in the assessment of mood disorder in the setting of physical illness. Whereas many rating scales have poor specificity for the disorder they are designed to assess, e.g. an anxiety scale containing a large proportion of items referring to symptoms of depressed mood and vice versa, inspection of the items comprising the MADRS and the CAS shows that there is little overlap (one of the ten items of the MADRS does refer to psychic anxiety, but this reflects the fact that anxiety is a frequent accompaniment of depressive states); despite this small overlap, the two scales have been shown to tap essentially different dimensions of mood disturbance (Snaith & Taylor, 1985a).

A major drawback to the practical use of both the MADRS and the CAS is that, neither in the original publications nor subsequently, have score ranges indicating different grades of severity of the mood disorder been presented. The present study has been conducted to rectify this deficit.

Method

The study to establish score ranges indicating different levels of severity of the mood disorders was carried out in a psychiatric department; this was necessary, since although the ranges of scores are intended as a guide to other clinicians, it is important to establish these on the basis of the requirement for treatment as usually recommended by psychiatrists. Thus, the 'recovered/absent' grade indicates no need for treatment, the 'moderate' grade a probable need for treatment, and the 'severe' grade an undoubted need for treatment of the mood disorder. Therefore, the data were collected from patients who were in-patients or out-patients at the adult psychiatric unit of St James's University Hospital. The data for the MADRS were based on ratings of patients whose diagnosis was depressive illness (Major Depressive Episode by the criteria of DSM III) and patients at all levels of severity were included, from very severely ill requiring urgent treatment, to the fully recovered. However, no patients were included who suffered from concurrent severe physical illness, schizophrenia, or organic disorder. About half were males and half females, and the age-range was 20 to 70 years. The data for the CAS were based on ratings of patients whose diagnosis was anxiety neurosis (both General Anxiety

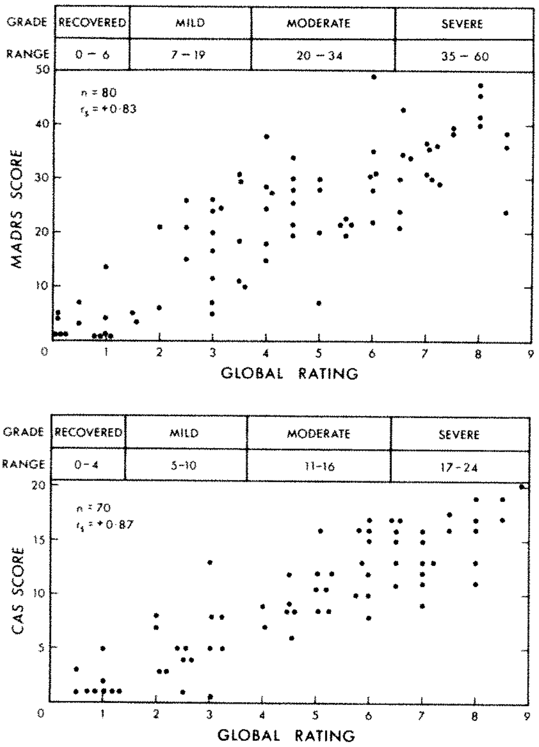

FIG. Score ranges in the severity grades of the MADRS and CAS.

Disorder and Panic Disorder by criteria of DSM III). Females accounted for about 60% of the sample, and the age-range was 18 to 60 years. Again, the full range of severity was included in the sample, including those patients who had recovered.

The ratings were conducted by the authors, who had undergone preliminary joint experience of the use of the rating scales and achieved consistency of ratings. Thereafter, two (in some cases one) raters made the global severity rating, and two other raters carried out the CAS or the MADRS at a separate session, but within 24 hours and in complete ignorance of the global assessment rating. The final rating was taken as the mean. The global assessment scale for depression was an 11-point (0–10) scale, but as noted in the earlier study (Kearns *et al*, 1982), the ultimate grade of severity is never used, since this indicates a severity of depressive illness characterised by such gross psychomotor disturbance (stupor) or loss of insight as would make the patient inaccessible to the use of rating scales of this type. The global assessment scale for anxiety was a ten-point (0–9) scale, in which it was possible, although rare, to be rated at the ultimate grade. The ratings were made on the basis of interviews lasting at least 30 minutes, in which the overall severity was assessed, not just at the moment of the interview, but over the past few days.

Results

Non-parametric statistical tests are used in the presentation of the data.

Overall grades of severity were defined by successive combinations of global rating scores so that approximately equal intervals were allotted to the four grades (a slightly smaller interval was used for the 'recovered/absent' grade on the depression scale, since it should be recognised that even very mild depressive disorder is worthy of consideration for treatment in clinical assessment). The figure present the scattergrams for the CAS and the MADRS with the proposed score ranges. These ranges were established on median scores between successive grades. The differences between grade scores were significant (by median tests) between all grades of both scales; the levels of statistical significance were at least at the one in twenty level, usually much higher, indicating that the scale scores distinguish satisfactorily between these grades.

Discussion

The score ranges established here may be used with confidence in future research and clinical practice. The two scales are brief enough to be used in tandem, thus providing measures of the severity of both mood disorders, with considerable advantages in assessment.

There is now an increasing awareness of mood disorder complicating physical illness and of the need for its detection and adequate treatment (Nabarro, 1984; Lloyd, 1985) and the establishment of a study section by The Royal College of Psychiatrists shows that psychiatrists are becoming increasingly aware of their contribution outside the confines of psychiatric departments and hospitals. Snaith (1981) has commented that observer scales, i.e. scales administered at examination by a research worker or clinician, are usefully supplemented by information from the patients' self-assessments. In this case, the Hospital Anxiety And Depression (HAD) Scale (Zigmond & Snaith, 1983) may be recommended, since it was specifically designed for use in general hospital non-psychiatric departments, and so far as possible, symptomatology likely to be influenced by concurrent physical illness, such as anorexia and pain, have been excluded. The HAD sub-scales have received validation against both the MADRS and the CAS (Snaith & Taylor, 1985a). For investigators who are particularly interested in the relationship of irritability of mood to depression and anxiety, the self-assessment scale known as the Irritability-Depression-Anxiety (IDA) Scale is recommended; information on its further validation is given in the survey of the relationship of irritability to other disordered physical and mental states (Snaith & Taylor, 1985b).

A future development may include a more thorough examination of the characteristics of CAS and the MADRS in the setting of physical illness, which may lead to further refinements in the detection and assessment of mood disorder in the setting of physical illness.

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*R. P. Snaith, MD, FRCPsych, *Senior Lecturer in Psychiatry.*
F. M. Harrop, BM, BS, *Senior House Officer.*
D. A. Newby, MA, MRCPsych, *Tutor in Psychiatry.*
C. Teale, BM, *Senior House Officer.*

Clinical Sciences Building, St James's University Hospital, Beckett Street, Leeds LS9 7TF.

*Correspondence

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Gilles de la Tourette's Syndrome in Down's Syndrome – A Case Report

Gilles de la Tourette's syndrome (GTS) is characterised by recurrent, involuntary motor and phonic tics that vary in intensity and begin between the ages of two and 15 years (American Psychiatric Association, 1980). The following case report documents its occurrence and treatment in an individual with Down's syndrome.

Case Report

The patient, a female, is 26 years-old and the youngest of three siblings. She was born to a 40 year-old mother and 45 year-old father, after an uneventful, full-term pregnancy, labour, and delivery. Her birth weight was 3.2 kgs. No neonatal complications were noted in the original hospital documents. There is no family history of relevant disabilities, including tics or other movement disorders.

Recognised to have Down's syndrome (DS) at birth, she was immediately institutionalised. Subsequent karyotyping (lymphocyte culture) revealed regular trisomy 21. The only developmental history available is that she walked at five years. At age 11, she was transferred to her current residence – a large rural institution for the developmentally handicapped. At that time, formal psychometric assessment showed profound mental retardation, with an

IQ of less than 20. Currently, she is able to dress herself with supervision, can feed herself with a spoon, and is only occasionally incontinent. Meaningful speech and gestures expressing her needs remain absent.

Her physical health remained excellent until age 23, when she developed pneumonitis and a right pleural effusion that responded to antibiotics. At the age of 24, her medical records indicate that she had two 'seizures', which were not clearly described. Investigation consisted of a skull x-ray, which showed a skull volume smaller than average but otherwise normal, and an EEG, which demonstrated "a diffuse slow dysrhythmia of moderate proportion"; the only previous EEG, at age 11, was "diffusely abnormal." Carbamazepine was prescribed (100 mg, tid) and no further 'seizures' have been noted. Her only other recent medication was an oral contraceptive agent (norethindrone acetate-ethinyl estradiol 2.5 mg/50 mcg tablets). Past medication consisted of small dosages of various major tranquillisers, barbiturates, hydroxyzine, and diazepam. In an institutional survey, she was found to be a HB_sAg carrier; liver function tests have remained normal.

The patient was recently noted to have frequent multiple motor and phonic tics; nursing staff confirmed that she had consistently displayed these behaviours at various intensities since her admission. They were observed to disappear during sleep and to increase in unfamiliar situations, as well as to interfere with her eating and social activity. The following representative comments were taken from a review of her medical notes: "frequently made snorting vocalizations, spat and exhibited much motor activity"; "she imitates freely and carries out a lot of sudden spontaneous snorting, snoring and yelping sounds." It was not possible accurately to correlate symptoms to her previous medications.

On examination, the patient exhibited the typical external clinical features of DS and a left esotropia. No other cranial nerve, motor, sensory or reflex abnormalities were detected. The simple motor tics observed involved muscles of the face, head, neck and shoulder areas, upper limbs, thorax, and abdomen. The following phonic tics were also observed: grunt, gasp, shriek, sniff, snort, spitting, unintelligible sounds, and bark. Both echopraxia and echolalia for sounds were present intermittently. She was responsive to affection.

In the absence of meaningful speech, sounds may represent voluntary attempts at communication; a conservative approach to identifying phonic tics was therefore adopted. Only those sounds that were associated in time with obvious motor tics (including sudden abdominal and diaphragmatic contractions) and did not seem at all related to external environmental stimuli were identified as phonic tics.

GTS was diagnosed according to DSM-III criteria, and pimozide was selected as a treatment because recent studies (Ross & Moldofsky, 1978; Shapiro *et al*, 1983) indicated that it is effective, with fewer adverse side-effects than haloperidol which has been the treatment of choice for some time (Woodbine, 1974); it was initiated at 1 mg per day, and increased at two to three-week intervals. Clinical response was judged from five-minute videotapes, filmed two to three times per week, during the patient's noon meal. On 20 mg pimozide/day, there was a dramatic reduction in both motor and phonic tics; this was confirmed by a rater who was blind to treatment and who scored the tapes in randomised order (see Fig. 1). As parkinsonian symptoms also developed on 20 mg pimozide/day, the pimozide was reduced to 18 mg/day, but tics reappeared. A combination of 20 mg pimozide/day and 6 mg benztropine/day was eventually found to provide good control of both motor and phonic tics, with limited extrapyramidal side-effects.

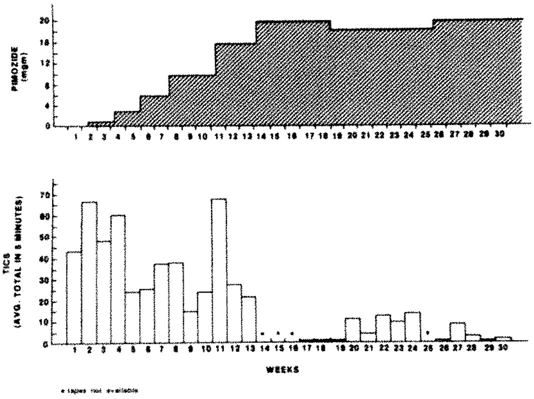

FIG. 1 Relationship between pimozide dosage and tic frequency.

Discussion

Gilles de la Tourette's syndrome has been described previously in a number of mentally handicapped individuals (Golden & Greenhill, 1981; Reid, 1984), as well as in three individuals with chromosomal anomalies: an XYY man (Merskey, 1974); a woman with XXX and 9p mosaicism (Singh *et al*, 1982); and a boy with fragile X syndrome (Kerbeshian *et al*, 1984). However, the only recorded possible association with Down's syndrome of which we are aware is that by Sacks (1982) of "a patient with mongolism who developed GTS at the age of 30, coincident with the appearance of thyrotoxicosis". The absence of previous reports of the association suggests that it is coincidental, but until recently, GTS has been overlooked even in the general population (Shapiro *et al*, 1978). Furthermore, mentally retarded individuals often display unusual mannerisms and/or vocalisations. Superimposed on this background, GTS (and other movement disorders) may be underdiagnosed, so that prevalence studies are needed to document GTS in DS, as well as other disorders associated with mental retardation.

If the association between some mental retardation syndromes and GTS proved not to be coincidental, then the presence of the disorder in these retarded individuals might contribute to a better understanding of its occurrence in the general population. Although the aetiology of GTS is uncertain, evidence for a postulated neurochemical abnormality, particularly involving the dopaminergic system, is persuasive (Feinberg & Carroll, 1979). Furthermore, pedigree studies in some patients with the disorder suggest genetic determination (Moldofsky *et al*, 1974; Comings *et al*, 1984). It is tempting to speculate that the excess genetic material present in our patient (trisomy 21) might distort particular biochemical pathways that underlie GTS. However, given the long history of intensive clinical investigations of DS, it is unlikely that the dramatic symptoms of GTS would have been overlooked in the significant percentage of individuals with DS that such a mechanism, if operative, would predict to be affected.

Gilles de la Tourette's syndrome and syndromes associated with mental retardation possibly could be linked for a theoretically different reason. Moldofsky *et al* (1974) suggested that irreversible neural structural changes may predispose to GTS. Data indicating an excess of abnormal EEGs, 'soft' neurological signs, psychological ratings of organic impairment, and left-handedness or ambidexterity in groups of individuals with GTS support this view (Shapiro *et al*, 1978). Sacks (1982) has described acquired Tourette-like syndromes in a variety of neurological disorders, and Golden & Greenhill (1981) remarked on the possible aetiological significance of underlying central nervous system abnormalities in mentally retarded patients with GTS. GTS in our patient might, therefore, be due to some neuropathological abnormality beyond the diffuse and non-specific changes that more commonly characterise DS brains. The overall rate of EEG abnormalities in DS is about 20%, with a reported incidence of epilepsy ranging from less than 1% to 10% of cases (Smith & Berg, 1976). Our patient had both a diffuse EEG abnormality and the history of a possible seizure disorder, which present in only a minority of individuals with DS. These may reflect a particularly severe or additional underlying central nervous system abnormality which could account also for GTS in this patient.

At present, though, it is uncertain whether persons with DS (or other mental retardation syndromes) may be at increased risk for the development of GTS.

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H. Karlinsky, MD, *Resident in Psychiatry, University of Toronto.*

P. Sandor, MD, FRCP(C), *Lecturer, Department of Psychiatry, University of Toronto.*

*J. M. Berg, MB, BCh, MSc, FRCPsych, FCCMG, *Director of Genetic Services and Biomedical Research, Surrey Place Centre, 2 Surrey Place, Toronto. M5S 2C2; Professor of Psychiatry and of Medical Genetics, University of Toronto.*

H. Moldofsky, MD, FRCP(C), *Professor of Psychiatry, University of Toronto.*

E. Crawford, MD, *Director, Medical Services, Huronia Regional Centre, Orillia, Ontario.*

*Correspondence

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Minimal Sedation Required with Nitrous Oxide-Oxygen Treatment of the Alcohol Withdrawal State

We have shown previously that nitrous oxide (N_2O) and oxygen (O_2) can be used successfully to treat the alcohol withdrawal state (AWS) (Lichtigfeld & Gillman, 1982). Our retrospective study of 500 cases showed that compared to routine treatment, when using the N_2O treatment, sedative medication could be cut enormously, and limited to night sedation only. This reduction occurred despite only one application of N_2O/O_2 being necessary in most cases. The purpose of this prospective study was to assess the sedation requirements of a group of patients treated with N_2O/O_2, and to compare these requirements with a similar group of patients treated with routine sedative medication.

Method

Subjects

Informed consent was obtained from 78 male subjects (mean age 34.2 years) who were matched for age, educational and social status, as well as chronicity of alcoholism. To qualify for this study, the time to the last drink had to have been greater than eight and no greater than 24 hours. Subjects were excluded if they showed evidence of chronic obstructive pulmonary disease or frank delirium tremens. They were then assigned to two groups in random order, i.e. either to the N_2O/O_2 or the routine sedation group.

Drug administration

Sedative medication or N_2O/O_2 was given on admission. All subjects received routine anti-epileptic medication (diphenylhydantoin). N_2O/O_2 was administered with a Quantiflex dental relative analgesia machine, as was previously described; briefly, 100% O_2 was given for 20 minutes, followed by 20 minutes of analgesic mixtures of N_2O/O_2 (i.e., low concentrations of N_2O diluted with high concentrations of O_2, where the O_2 concentration is never less than 30% of the gas mixture delivered to the patient). This was followed by 20 minutes of 100% oxygen to wash out residual N_2O.

Only a single treatment with N_2O/O_{2n} (at admission) was used in this study, and in any case, it has only been found necessary to administer the gases a second time in severe withdrawal (Lichtigfeld & Gillman, 1982). The Quantiflex machine has a fail-safe device, which halts the flow of N_2O, when the O_2 flow rate drops below 30%. Since this is an open circuit system (i.e., only using a nasal mask), anaesthesia is virtually impossible to produce.

Medication for the sedative group (i.e., who received no gas at admission) was administered by staff who were not directly involved in the study, and consisted of 5 mg diazepam tds (days one to three) and 2 mg diazepam tds (days four to seven).

Assessment of medication required

Medication requirements were assessed by experienced medical and nursing staff who were kept blind to the subjects' treatments at admission. In view of the obvious difficulty in maintaining the blind procedure, 22 patients who entered the trial are not included in the results, because the assessing staff became aware of the subjects' initial treatment.

Both groups of patients were monitored on succeeding days and given additional medication as required, using clinical assessment as the criteria for drug administration.

Results

The aggregate drug requirements for each group were as follows: *medication alone group*—phenobarbitone (30250 mg), oxazepam (7650 mg), chlormethiazole (4800 mg), diazepam (290 mg); *nitrous oxide group*—phenobarbitone (3200 mg), oxazepam (4960 mg), chlormethiazole (1920 mg), diazepam (50 mg).

Apart from the obvious and considerable decrease in sedation required, the length of treatment was also diminished. Using a one-tail Chi-square test from day three to seven, and comparing the two experimental groups, the hypothesis of no difference between the two groups can be rejected at the one per cent level. Hence, there is a significant difference between the groups on sedation and the 'gas group' with regard to length of sedation.

Furthermore, in order to eliminate bias, although standard medication was continued in the sedation alone group up to and including day seven in all cases, this medication (5 mg diazepam tds days one to three, and 2 mg diazepam tds days four to seven) was not taken into account in either the aggregate drug requirement score (above) or in the statistical analysis i.e., *only the additional medication was scored.* Where subjects were treated with N_2O/O_2 mixtures, they usually required 60 mg oxazepam nocte (days one to two), followed by oxazepam nocte 30 mg (days two to five). It was unusual for N_2O/O_2 treated patients to require medication on the six or succeeding night.

Discussion

Barbiturates and benzodiazepines have become the most commonly used agents for the treatment of AWS (Hemmingsen *et al*, 1979). Apart from the obvious difficulty of establishing the correct dosage of these agents for each individual, there are other problems associated with the use of these agents. Barbiturates have a relatively low therapeutic index, and can interact with large numbers of drugs (Harvey, 1980). In addition, both barbiturates and benzodiazepines have an abuse potential (Madden, 1979). Moreover, these drugs are capable of producing physical dependence (Harvey, 1980; Brandon, 1975).

Although benzodiazepines have a higher therapeutic index than the barbiturates, they share with the latter a large number of side-effects such as depression of psychomotor and cognitive function, development of tolerance, and an additive effect with other CNS depressants including ethanol (Harvey, 1980). In addition, cross-tolerance can develop between the benzodiazepines, the barbiturates, and ethanol (Harvey, 1980).

In contrast, *analgesic* concentrations of N_2O have been shown to be extremely safe (Gillman, 1982); in fact, many millions of administrations (in dentistry) have been provided without a single case of a serious side-effect ever being reported (Ruben, 1972).

Apart from the obvious financial savings inherent in a treatment requiring less nursing and fewer drugs (which is of particular importance in a developing African country such as ours), there are other advantages associated with the N_2O/O_2 treatment. One of the most important of these is the rapid amelioration of the patient's condition, which occurs within minutes of the treatment being instituted. This almost immediate therapeutic effect renders the subject more amenable to positive psychological manipulation, which is likely to be of great importance in treating the AWS (Lichtigfeld & Gillman, 1982; Hemmingsen *et al*, 1979; Sparadeo *et al*, 1982).

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*M. A. Gillman, BDS, MSc, DSc, *Director, South African Brain Research Institute, Suite 9, NBS Centre, Highland House, 173 Louis Botha Avenue, Orange Grove 2192, Johannesburg, South Africa, and Senior Lecturer, University of the Witwatersrand Medical School, Department of Experimental and Clinical Pharmacology.*

F. J. Lichtigfeld, MBBch, BSc, FF Psych (SA), *Director, South African Brain Research Institute, and Psychiatrist.*

*Correspondence

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One Hundred Cases of Hysteria in Eastern Libya

A Socio-Demographic Study

Although the concept of hysteria can be traced back some two and a half thousand years (Lewis, 1975), its validity as a psychiatric entity has been questioned (Szasz, 1961; Slater, 1961, 1965). Nevertheless, the terms 'hysteria' and 'hysterical' are still widely used, if not misused, in everyday medical practice. Possibly as a result of its opponents and the increasing sophistication of society, the use of 'hysteria' as a diagnostic label has declined considerably in Western countries. For example, in the out-patient department of the Bethlem & Maudsley Hospitals, London, 223 out of 6229 cases (3.5%) were diagnosed as 'hysteria' in 1955–57, but in 1967–69, only 45 out of 8585 cases (0.5%) were so diagnosed (Hare, 1969). However, in developing countries such as India, hysteria still continues to be a common diagnosis, applied to about 6–11% of all psychiatric out-patients (Wig *et al*, 1982). In Libya, the diagnosis of hysteria appears to be equally common. The symptoms presented by the patients are dramatic, with fits, paralysis, blindness, or aphonia predominating – symptoms rarely seen in the West nowadays. The aim of this paper is to study the socio-demographic and clinical features of such patients, and describe their management.

Method

The sample consisted of one hundred consecutive cases of conversion hysteria referred to the Benghazi Psychiatric Service for the first time between November 1983 and July 1984. 'Conversion hysteria' was operationally defined as the occurrence of a neurological symptom with no demonstrable structural lesion, but associated with an obvious significant emotional problem. All the cases were referred from the Neurology Unit of the Department of Medicine, from polyclinics, from the Army Hospital, or from the peripheral hospitals of Benghazi (a polyclinic is an out-patient clinic for all medical and surgical specialties, sited outside the hospital).

The patients were interviewed first by just one of us, using a semi-structured interview schedule prepared for this purpose. After the relevant history, socio-demographic and clinical data were recorded, all of us conducted a joint interview, after which the diagnosis and line of management were mutually agreed. Doubtful cases or those which did not command unanimity of diagnosis were excluded. All cases received supportive psychotherapy at least once. The Eysenck Personality Inventory (Arabic version) was given to those patients who could read and understand the questions.

Results

1. *Sex and age*

The sample comprised 40 males and 60 females, with a mean age of 20.2 years (s.d. 6.4; range 11–55). This group represented 8.25% of all first attenders at the out-patient clinic during the period, a rather high proportion compared to London, but quite in line with the Indian studies. The sex ratio of the sample (40%M:60%F) differed significantly from both the rest of the out-patients (67%M:33%F; $P<0.001$) and the catchment population (54%M:46%F; $P<0.01$) (Census & Statistical Dept of Libya, 1974). Moreover, 76% were under the age of 21, compared with only 21% of other out-patient first-attenders. This very significant difference in age ($P<0.001$) is similar to that found by Okasha (1969) in Egypt.

2. *Educational status*

The levels of education achieved were: illiterate 8%, primary 22%, preparatory 44%, secondary 21%, university 5%. The low illiteracy rate reflects the young age of the group and the recent enforcement of compulsory education in modern Libya; but although 92% were literate, only 65% could complete the Eysenck Personality Inventory (Arabic version) because of difficulty in comprehension (details to be published in a separate study of the hysterical personality). It has already been established that hysteria is more common in people with limited education (Mathur, 1975; Subramanian *et al*, 1980).

3. *Marital status*

Only 6 males (15%) and 15 females (25%) were married. In the Indian studies of hysteria, married subjects predominated, and it was concluded that family life increases the stress on the married individual (Mathur, 1975; Subramanian *et al*, 1980). The contrary finding in our series probably reflects the later age of marriage in Libya.

4. *Occupation*

Of the males, 60% were soldiers and 12.5% were students. Since military service is compulsory in Libya, the majority of young men are either soldiers or students. Murphy (1981) has noted that hysteria is more common in soldiers and subordinate males than in those who have had more opportunity to take decisions for themselves.

Among the females, 45% were students and 35% were either housewives or unmarried girls staying at home and performing household duties.

5. *Stress*

Patients were regarded as being under stress if they had experienced a painful life situation shortly before the onset of symptoms. Some, however, had more subtle stresses of longer duration. In males, the common stresses were: conflicts at work (50%); conflicts at home (12.5%); and love problems (12.5%). In females, they were: conflicts at home (26%); exams (18%); household responsibilities (12%); bereavement (10%); and love problems (8.5%). In only one male and two females was no stress detected.

Some examples will illustrate the kind of stressful experiences that preceded the onset of symptoms. A young unhappily married housewife who heard that her soldier brother had been posted to the front line developed fits. An immigrant worker, who had left his family behind, quarrelled with a fellow worker and developed convulsions. A not-very-bright student facing an examination developed aphonia when her teacher asked her to recite a difficult poem which she had failed to memorise. Another student preparing for examinations developed severe headache and became blind the next day. A foreign-born housewife who suspected that her husband was planning to marry his former girlfriend suddenly lost consciousness on seeing her coming to their house, and later became aphonic and hemiplegic.

6. *Symptoms*

The commonest presenting symptom was fits (72.5% of males, 50% of females). These consisted of wild disorganised threshing movements of the limbs and writhing of the trunk. Some patients had received intravenous diazepam before reaching us, so that their wild movements had disappeared, but they often remained in a stupor and responded only after application of strong unpleasant stimuli.

The next most frequent symptoms were paralysis and paresis (15% of males, 26.5% of females), followed by blindness (5% of males, 10% of females), aphonia (2.5% of males, 5% of females), and involuntary movements (2.5% of males, 5% of females). By contrast, Okasha (1969) found that amongst Egyptian hysterical patients, fits occurred in a higher proportion of females than males, and vice versa for paralysis.

The choice of symptom was sometimes symbolic in nature. For example, one young soldier was looking at a photograph of his girlfriend, whom he had not seen for two years, when he began to weep and suddenly lost his vision. More often, however, the choice was determined by the individual's past experience or by his experience of illness in others, as noted by Kendell (1974). Of our patients, 90% had a history of previous hysterical episodes, with similar symptoms in 51%. The remaining 10% had no previous psychiatric history.

Three patients with fits had an abnormal EEG, but the attending neurologist made a diagnosis of pseudo-seizure.

Some subjects had observed their symptoms, either organic or hysterical, in close relatives or associates. Seven males and twelve females reported mental illness in the family, and the majority of these cases were probably hysterical.

Management

All the patients, except three who recovered spontaneously, received psychotherapy in the form of support, explanation, education, and suggestion to remove the symptom: 55% of them needed additional anxiolytic or antidepressant therapy for a period of 1–6 weeks. Three males and four females had to be given extracephalic electrical stimulation (to the leg in six cases and the arm in one, in addition to psychotherapy and drugs, before limb movement was restored. One case of paralysis, treated unsuccessfully with extracephalic stimulation by another doctor, recovered after psychotherapeutic suggestion. On the whole, we prefer psychotherapy to electrical stimulation because the former leads to a better patient–therapist relationship. Only a few patients needed more than one session of psychotherapy.

Outcome

Systematic follow-up was not possible as patients could rarely be persuaded to attend once they had recovered. They could, however, be expected to return if their condition recurred.

One male and two females recovered spontaneously. All patients became symptom-free, in the short-term, after treatment. Some of the patients with fits, especially the soldiers, returned with further attacks. One ptosis patient had an attack of fits two days after recovery from the ptosis. One blind girl was reported to be blind again, one week later, but did not return for treatment since she had left the area. Only one case of paralysis relapsed, within a month, but recovered after extracephalic stimulus therapy.

Discussion

Hysteria, derived from the Greek word 'Rysteron', was recorded in ancient Egypt in the Kahun papyrus as a series of morbid states attributable to the wandering of the uterus in the body (Veith, 1965). Based upon this false notion of pathology, the condition was still considered, until lately, to be an illness of sexually unsatisfied females: males were not supposed to suffer from hysteria. Even during the First World War, hysteria, a very common disorder among front-line soldiers, was recognised only as 'shell shock' (Merskey, 1979). Our study shows that although women significantly outnumbered men, quite a large proportion of subjects were males.

Freud postulated that hysteria is an illness resulting from unconscious mental conflicts: the symptoms solve the conflicts, which are often too unpleasant to be faced or resolved at the conscious level (Freud, 1909, 1917). This he described as the *primary gain* of hysteria. *Secondary gain* represents the advantages that the patient may obtain, such as care, extra attention, nursing, avoidance of responsibilities, etc. These can in turn reinforce the hysterical mechanism and maintain the symptom. Non-hysterical patients can also develop secondary gain, and their physical illness may be unduly prolonged: non-psychiatric doctors often tend to label such cases as hysteria or hysterical.

One contention of the Freudian concept of hysteria is that the motivation for symptom development must be unconscious: conscious motivation indicates malingering. In practice, it is almost impossible to distinguish the two, and motivation is often partly conscious and partly unconcious. In our series, it was obvious that all the blind patients could see, all the paralysed patients could move, and all the aphonic patients could talk, if they really tried. After persuasion and psychotherapeutic suggestion, all could perform these actions. The reason behind the blindness, paralysis, or aphonia could possibly be that they did not *want* to see, move, or talk. The state 'I wish not' leads to 'I will not' and later to 'I cannot'. All the patients were easily suggestible, and auto-suggestion may play an important role in the development of symptoms.

Whether or not hysteria is a disease *sui generis* is another question. Slater (1965), is often quoted as remarking that 'All the signs of hysteria are the signs not of disease, but of health'. Nevertheless, without appropriate help, these patients can remain incapacitated for a long time. We noted that almost all the patients in the sample had been facing an unpleasant life situation which could not be resolved. Like parasuicide, the development of hysterical symptoms can be viewed as a cry for help. In our culture, bodily ill-health is more respectable and acceptable than emotional symptoms, and only by the dramatic appearance of such ill-health can patients gain attention quickly. Thus, conversion hysteria can be viewed as 'illness behaviour' in a person under emotional stress: the dramatic appearance of physical ill-health is his means of communicating to others that he is in distress and needs help. Because of the absence of a physical lesion, doctors often tend to ignore such a patient; on the other hand, some doctors, unable to find the cause or remove the symptom, may over-investigate and thereby provide secondary gain. In our view, both courses of action are harmful and must be avoided. In our study, every patient showed relief of the presenting symptoms after a small number of psychotherapeutic sessions (in some cases just one): such therapy is within the competence of every doctor prepared to devote the necessary time and attention to the patient.

Acknowledgement

We thank the consultants in the Neurology Unit of the Department of Medicine and our colleagues at the Benghazi Psychiatric Hospital for their kind cooperation in this study. We also thank Dr Kenneth Davison, visiting Professor of Psychiatry, for his critical review, comments and valuable suggestions. Our thanks are also due to Mrs C. Apatt for secretarial help.

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*Tinnyunt Pu, MBBS, MRCPsych, *Assistant Professor of Psychiatry, Faculty of Medicine, Garyounis University, Benghazi, Libya:* Postal address *P.O. Box 7646, Benghazi, Libya.*

E. Mohamed, MA, DM & SP, *Lecturer in Clinical Psychology, Faculty of Medicine, Garyounis University, Benghazi, Libya.*

Kareema Imam, BA, DipEdPsy, *Clinical Psychologist, Benghazi Psychiatric Hospital, Benghazi, Libya.*

Ali M. El-Roey, MB, ChB, MSc (Psych), *Lecturer in Psychiatry, Faculty of Medicine, Garyounis University, Benghazi, Libya.*

*Correspondence

(Accepted 1 March 1985)

British Journal of Psychiatry (1986), **148**, 610–616

Correspondence

Psychotherapy and Placebo

SIR: Dr Mowbray (*Journal,* March 1986, **148,** 337–338), suggests that "since the effects of placebo are psychological and the treatment in question (psychotherapy) is also "psychological" then we are simply comparing like with like—psychological with psychological". I think Dr Mowbray fails completely to understand the point I was trying to make in stating that placebo treatment was as successful as psychoanalysis or psychotherapy in general (but less so than behaviour therapy) in the treatment of neurotic patients.

The claims which have been, and are still being made for the various types of psychoanalytic and psychotherapeutic treatment are based on the theory that the treatments are in some way "specific" i.e., are derived from a more general theory of neurosis, and therefore are superior to other treatments not so derived, or derived from some alternative or inferior theory. This view was most clearly expressed by Freud, with respect to psychoanalysis, but it is equally held by the many other authors who favour alternative therapies.

The demonstration that placebo treatment which is by definition not only not derived from any specific theory, but expressly is defined in such a way as to exclude such specific influences as inform the therapy with which it is being compared, is equally successful in curing or ameliorating the disorders of neurotic patients clearly disproves any such claims for "specificity". Furthermore, if placebo treatment is as effective as psychoanalysis and psychotherapy in general, then why bother to spend years training psychoanalysts and psychotherapists, when this training clearly adds nothing to their efficacy? Indeed, Smith, Glass and Miller (1980), in a book often cited as proving the value of psychotherapy, found that duration of training of the therapist correlated zero with the efficacy of the treatment!

The only treatment which emerged as clearly superior in the varied comparative studies that have been done is behaviour therapy, suggesting that it alone has a specific effect which is related to the theory on which it is based (Eysenck, 1959). It is no doubt for this reason that behaviour therapy is being used more and more widely in the treatment of neurotic disorders.

H. J. EYSENCK

Institute of Psychiatry
De Crespigny Park
Denmark Hill, London SE5

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Anniversary Reactions

SIR: Renvoize & Jain's Brief Report (*Journal,* March 1986, **148,** 322–4) perpetuates a confusion which I (1981) tried to correct. An anniversary reaction should strictly speaking be the onset, or intensification, of symptoms at or about the anniversary of a significant past event, which was probably (though not necessarily) stressful. Such a reaction can occur each time the anniversary comes round, though it is likely to be most intense on the first anniversary. It has much in common with a delayed grief reaction and may well represent the expression of emotion which had been held back at the time of the original event.

Most of the examples presented by Renvoize & Jain are what, more correctly, should be described as age-correspondence-precipitated reactions. These occur when the subject, or a close relative of the subject, reaches an age which corresponds with a time when a specific tragedy occurred to another person. This most likely represents a degree of identification with this other person, and is either a fear that the same tragedy will befall the subject, or an enactment, by the subject, in fantasy or reality, of the original tragedy. The distinguishing feature of the age-correspondence-precipitated reaction is that it can occur only once, namely when the two ages correspond.

Renvoize & Jain maintain, though with no supportive evidence, that anniversary reactions are "probably quite common". True anniversary reactions, such as occur to widows or widowers one year after their partners' death (Bornstein & Clayton, 1972) probably are common, though are mostly so mild as not to require the attention of psychiatrists. My own study suggests that age-correspondence-precipitated reactions are rare. When they do occur it is important that they be recognised as such, since they can sometimes present as florid psychotic states (Hilgard & Newman, 1959). I would be interested to know if any readers have experience of one.

JOHN BIRTCHNELL

MRC Social Psychiatry Unit
Institute of Psychiatry
De Crespigny Park
London SE5 8AF

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Depression and Urinary Free Cortisol

SIR: B. J. Carroll (*Journal*, February 1986, **148**, 218) questions the use of the radio-immuno assay (RIA) procedure and suggests that the urinary free cortisol (UFC) levels were unusually high in the patients in our study (*Journal*, October 1985, **147**, 429–433). He states that the values were "all well within the range expected for patients with Cushing's Disease".

In fact, only 38 of the 72 patients had a 24 hour UFC secretion above the normal range (25–130 µmg/24 hours). The mean pre-dexamethasone 24-hour UFC was 158.6 µgm/24 hours (SD = 77.8, range 33–378) which was higher than that found by Diegbold *et al* (1981) (mean = 122 µgm/24 hours). One likely explanation for this is the fact that the patients in our study were essentially drug free in comparison to the above study and that of Carroll *et al* (1976) in which patients were treated with psychotropic medication, including benzodiazepines, which have been shown to lower cortisol levels.

The NIMH study (Stokes *et al*, 1984) on drug-free patients reported mean pre-dexamethasone UFC levels of 148 µmg/24 hours in unipolar depressed patients, a result very similar to our own. Moreover, the post-dexamethasone UFC results in the two studies were remarkably similar with the NIMH study reporting levels of 59 µgms per 24 hours, (and 65 µgm per 24 hours in patients with unipolar depression), as compared to 65.4 µgm per 24 hours in our study of mainly unipolar depressed patients (Calloway *et al*, 1984).

Carroll also questions the validity of using RIA for measuring plasma cortisols in the DST. It has been established that RIA gives comparable results to competitive protein binding (Wilens *et al*, 1983) and RIA is now the most widely used method for assaying cortisols in DST studies of depressed patients (e.g., Stokes *et al*, 1984).

S. P. CALLOWAY

Fulbourn Hospital, Cambridge CB1 5EF

R. J. DOLAN

Maudsley Hospital, London

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Pseudodementia: Facts and Figures

SIR: The article by Drs Bulbena and Berrios (*Journal*, January 1986, **148**, 87–94) referred to the fact that speculation abounds in relation to the concept of pseudodementia. We decided to examine their observation "that there is no consensus on the use and application of the diagnosis of 'pseudodementia". We will avoid commenting on how one *diagnoses* a presentation. We were also interested in seeing how closely our findings approached their "stringent criteria"—cognitive impairment of the dementia-type, absence of a relevant organic disorder, and reversibility.

We sent questionnaires, a covering letter, and s.a.e's. to a random sample of Irish psychiatrists of senior status ($n = 65$). We placed a five week deadline for the return of correspondence. Twenty-nine questionnaires were returned.

The questionnaire consisted of three questions. The answers given to these, including only those given by more than one respondent (absolute numbers in brackets) were as follows:

1. What do you understand by the term pseudodementia?

Resembles an organic dementia (18), potentially reversible with/without treatment (6), functional (9), depressive (9), found usually in elderly (5), memory impairment an important component (12), and "hysterical", including Ganser's syndrome (7).

2. What do you consider to be its cause(s)?

Depression, especially in the elderly (21), anxiety/stress/loss (8), "hysteria"—dissociative (7), "Ganser's syndrome" (3), schizophrenia/schizophreniform (5), malingering (2). Parkinsonism, hypovitaminoses, hypothyroidism and other metabolic causes, and "age-related brain changes" were mentioned by individual respondents.

3. Please comment on the current use and validity of the term.

A reminder to the physician to search further (6), a retrospective diagnosis—with or without the use of treatment (4), a useful term if criteria are stated (4), should be confined to elderly depressives with a dementia-like syndrome (3), a useful term (3), a useless/confusing term (3), a term of rare applicability (3), and, lest we forget, depression and dementia may co-exist (2).

Our general impression was that pseudodementia, like "pseudodepression" (Feinberg & Goodman, 1984), is a loosely held concept amongst psychiatrists. We would suggest that it be replaced by a clearer statement of the findings. As an illustration of how this might be done we would refer to Feinberg & Goodman's (1984) "four 'Ideal Types' of depression plus dementia syndromes": depression presenting as dementia ("depressive pseudodementia"), dementia presenting as depression ("pseudodepression"), depression with secondary dementia ("dementia syndrome of depression"), and dementia with secondary depression ("depressive syndrome of dementia").

Brian O'Shea
Martin Rahill
Catherine McCollam

Newcastle Hospital
Greystones
Co. Wicklow

Reference

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Huntington's Chorea Without Dementia

Sir: We would like to comment on the case report of Turner (*Journal*, May 1985, **146**, 548–550) concerning a patient who developed chorea in middle age, had a positive family history of Huntington's chorea, but who showed no evidence of dementia on formal psychological testing. The author questions the value of genetic counselling in this case and in particular whether it was justified, given that there were doubts about the diagnosis. We agree that the likely diagnosis for this patient is Huntington's chorea and would not be surprised by the lack of dementia, particularly with a relatively late age at onset. Indeed, lack of mental deterioration in some cases was noted by Davenport & Muncie (1916). Caution is required if there is a family history or non-progressive choreiform movements from childhood without dementia, since a likely diagnosis is benign hereditary chorea (Harper, 1978).

Genetic counselling should be part of the management of any family in which a relative is diagnosed to have Huntington's chorea, and the consequences of its deficiency are well documented by Martindale & Yale (1983). The form of the counselling is important and a general family meeting is inadequate; risks for an individual need to be considered separately and worries and fears dealt with on an individual basis. We question the statement that the seven living siblings had outlived their major risk period, since 10% of Huntington's chorea patients have an age of onset after 60 years (the age of the eldest sibling). The risk to the youngest sibling aged 42 years is considerably higher—approximately 38%, based on the life table method of Newcombe (1981).

Concern was expressed about the daughter of the index case, who may have broken off her engagement for a number of reasons. A full discussion of the genetic aspects might have eased her problem; in particular, information about the recent developments in DNA technology which may allow her to have children at low risk for developing Huntington's chorea, without changing the risks to herself (Harper & Sarfarzi, 1985).

O. W. J. Quarrell
Peter S. Harper

University of Wales College of Medicine
Department of Medicine
Heath Park
Cardiff CF4 4XN

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Treatment of Mania with the Cholinomimetic Agent RS 86

SIR: According to observations that cholinomimetic agents such as physostigmine may counteract mania and can cause depression, Janowsky (1972) formulated the cholinergic-adrenergic imbalance hypothesis of affective disorders. It postulates that depression is due to a central nervous hyperactivity of the cholinergic system in relation to the adrenergic system and that the opposite is the case for mania. In contrast to physostigmine, which has a half-life of only 10–20 minutes and the injection of which is frequently accompanied by unpleasant vegetative side-effects requiring the application of the peripherally acting antidote methscopolamin, the spiropiperidyl derivative RS 86 is a more suitable drug for studying the question of whether cholinomimetic agents possess an anti-manic effect. RS 86 is a direct muscarinic agonist, passes the blood brain barrier, has a half-life of six to eight hours and because of the drug's minor peripheral side-effects its combination with an antidote is not necessary (Spiegel, 1984).

In a double-blind study, using a placebo-drug-placebo-drug design, RS 86 was given to six female and four male patients aged between 19 and 52 years (mean = 35.6, SD = 10.6); nine patients fulfilled the RDC for mania, one for hypomania. The length of the placebo phases varied from two to seven days; the drug phases lasted six days with a successive increase of the doses generally up to 4 mg RS 86 per day. If clinically necessary, chloral hydrate, paraldehyde or levopromazine (maximally 400 mg per day) were administered. The degree of mania was assessed daily by two independent raters using the Inpatient Multidimensional Psychiatric Scale (IMPS) (Lorr, 1974).

Three patients did not show any improvement in their manic syndrome after the intake of RS 86. In one of them, even the increase of the dosage up to 6 mg had no effect on the psychopathology but caused nausea. Two patients displayed a marked improvement of the manic disorder during the drug phase, a relapse during the following placebo phase, and once again an improvement in the second drug phase. Five patients experienced a continuous improvement in their manic symptomatology which also lasted throughout the following placebo phase. As indicated by the relevant IMPS items, the improvement of the manic symptoms, which was observed two to four days after RS 86 intake, included not only psychomotor disturbances but also euphoria, grandiosity and superiority. Except for the nausea reported by the one patient who did not even respond to the 6 mg RS 86 dose, only minor side-effects such as increased salivation or sweating were reported.

Our study confirms former findings that cholinomimetic agents possess antimanic properties. The lack of effectiveness of RS 86 in three of the ten patients cannot be explained by the fact that the non-responders suffered from a more severe manic psychopathology than the responders, as this was not the case. A different pathogenetic mechanism, not influenced by the muscarinic agonist, or individual differences in the bioavailability of RS 86 might be responsible for the varied clinical responses. Surprisingly, five of the seven RS 86 responders did not show a relapse during the second placebo phase. As a spontaneous remission occurring in each of these patients during the first days of RS 86 medication seems to be rather unlikely, a RS 86 induced "switch process" terminating the manic episode has to be considered.

J. C. KRIEG
M. BERGER

Max Planck Institute of Psychiatry
Kraepelinstr. 10
D-8000 München 40
West Germany

References

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Is Mania Really Incompatible with Down's Syndrome?

SIR: As we were already surveying the Down's syndrome population of our hospital, for psychiatric illness, we were very interested in the observation of Sovner *et al* (*Journal*, March 1985, **146**, 319–320). Their hypothesis that Down's Syndrome precludes the development of mania enhances our understanding of the aetiology of psychosis.

We identified 60 cases of Down's syndrome from among a hospital population of 1014. Apart from the Standard Psychiatric Interview we used Feigner's criteria and ward staffs' observations in diagnosing mania. We also looked at the old case notes to see if there had been any evidence of mania or periodic behaviour disturbance. We only found one case, a male aged 40, who displays cyclical mood change. He becomes boisterous, argumentative, and slightly euphoric every 15 days or so. This lasts for a couple of days to one week, and then he is more manageable. He has not needed any neuroleptic medication to control his symptoms. The rest of the cases did not show any evidence of hypomania or mania. Our study seems to confirm the Sovner *et al* hypothesis that Down's syndrome precludes the expression of mania.

In a study of six cases of Down's syndrome, brains were studied at autopsy (Mann *et al,* 1985). Nerve cell loss and reduction in nucleolar volume were found in the noradrenergic system of the locus caeruleus and dorsal motor vagus, the cholinergic system of the nucleus basilis and the serotonin system of raphe nuclei, whereas only slight change occurred in the dopaminergic system of the substantia nigra. Yates *et al* (1983) studied the brain of a 27 year old patient with Down's syndrome (in whom plaques and tangles were absent) and showed choline acetyl-transferase and acetylcholine esterase activities to be normal, dopamine content to be normal, but noradrenaline content to be reduced. Although the biochemical studies on mania are conflicting, if mania is due to abnormal noradrenergic metabolism, then the evidence of damaged noradrenergic system in Down's syndrome can explain the lack of manic cases.

IQBAL SINGH
G. ZOLESE

*Leavesden Hospital
Abbots Langley
Herts WD5 0NU*

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Thirty Month Follow-Up of Cognitive-Behavioural Group Therapy for Bulimia

SIR: Both controlled and uncontrolled studies suggest that cognitive-behavioural treatment, administered either individually, or in group format, is useful in the treatment of bulimia (Fairburn, 1981; Lacey, 1983; Kirkley *et al,* 1985). We report a thirty month follow up of 10 bulimic women who received group cognitive-behavioural therapy for 16 weeks (Schneider & Agras, 1985). These women (10 of the original 13 participants) had induced vomiting about 16 times each week before treatment, a rate that was reduced to about once a week post-treatment, with six of the ten women being abstinent. These women were interviewed by one of us and various standardised psychological tests were administered.

We found that the mean rate of self-induced vomiting had increased to 4.1 episodes per week at thirty months post-treatment. The scores on the Beck Depression Inventory (BDI) (10.1 post-treatment and 10.2 at 30 month follow-up) as well as clinical observation, suggest that the improvement in depressive symptoms was well maintained. Those who had stopped vomiting had a mean BDI of 5.2, while those who continued to vomit had a BDI of 15.2. Pre-treatment BDI scores for these two groups were similar: 29 for those who stopped vomiting, and 25.2 for those who continued. Attitudes toward eating improved from post-treatment to 30 month follow-up (Eating Attitudes Test (EAT) mean scores 25.6 versus 16.3). This finding is confirmed by a slight rise in the mean ideal weight reported by these patients from before therapy to 30 month follow-up. Those who stopped vomiting had a mean EAT of 11.75 and showed a mean rise in ideal weight of 4.8 lbs, while those who continued to vomit had a mean EAT of 20.75 and showed a decrease in ideal weight of 2.6 lbs.

These results suggest that there is reasonable long term maintenance of improvement for bulimic women treated with group cognitive-behavioural therapy. An examination of the post-treatment and six month follow-up data suggest that the major tendency for relapse occurs during the first six months following treatment, and that thereafter there is reasonable maintenance. There are, however, differences between those who continued to induce vomiting and those who stopped. In particular, those who stopped vomiting report less depression, have a lower EAT score, and report an increase in ideal weight. On the other hand, neither the BDI or the EAT scores were different for these two groups pre-treatment.

These results are in accord with those of Lacey (1983), who followed his patients for two years post-treatment and reported stability of outcome over that time. These long-term results must be confirmed with a controlled outcome study; nonetheless they suggest that cognitive-behavioural treatment produces lasting benefits for bulimic women. From a clinical viewpoint, it appears that relapse prevention strategies need to be pursued actively for the first few months following the completion of treatment.

LASZLO P. LUKA
W. STEWART AGRAS
JOHN A. SCHNEIDER
Stanford University School of Medicine
Stanford, California 94305

References

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Blood Alcohol Survey in Patients with Self-Poisoning

SIR: One hundred and fifty-eight consecutive admissions for self-poisoning were studied for alcohol use in an Accident and Emergency Department. Forty-one per cent of the case population had blood alcohol present and 29 per cent had levels exceeding 17.4 mmol/l (80 mgm/100 ml) These findings are similar to those from a study by Holt *et al* (1980) of casualty attenders at a teaching district general hospital. Our results also showed that blood alcohol levels were higher in older patients (40+) ($r=0.25$, $P<0.01$) for both sexes. The association of sex with a weekday/weekend variable was significant ($\chi^2=5.72$, $df=1$, $P<0.05$): higher blood alcohol levels were associated with female self-poisoners on weekdays and with male self-poisoners at weekends. Blood alcohol levels of women arriving during "risk" times (2200–0659 hours) were significantly higher than those of women arriving at the other times ($t=3.45$, $df=92$, $P<0.001$). These variations between the sexes deserve further study.

The intoxicated patient presents a diagnostic challenge to the casualty officer since the contribution of alcohol to the clinical state may make the assessment critical, especially in self-poisoning cases. This also becomes important in the early evaluation and management of psychological distress. Although the association of alcohol intoxication and suicidal risk has been well documented (e.g., Barraclough *et al*, 1974), the extent of this association becomes ambiguous if information on the level of intoxication is obtained through self-report.

Our results alert us to the need for providing better psychiatric back-up services in the assessment and management of these patients. We may have to place greater emphasis on the subject of alcohol abuse and comprehensive assessment of self-poisoning cases in the training of junior physicians. Brief alcoholism questionnaires (Wanberg *et al*, 1979) may be used in selected cases where there is a suspicion of dependency. Immediate counselling or therapy, especially for self-poisoners with higher levels of neurotic symptomatology, should be arranged to tackle the alcohol abuse problem (Newsom-Smith & Hirsch, 1979). There is a strong case for integrating alcoholism treatment services with accident and emergency department services

R. VARADARAJ
St Augustine's Hospital, Canterbury
J. D. MENDONCA
Crisis & Short Term Intervention Unit
St Thomas Psychiatric Hospital
St Thomas, Ontario
Canada

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Schizophrenia and the Media

SIR: I write, as a retired psychiatrist, to suggest that psychiatrists could use and add to the present publicity on schizophrenia.

"The most disabling illness known to mankind" is how *The Times* referred to schizophrenia after months of informed articles and correspondence. "The most heart-rending assignment I have ever had. I could not believe that people in Britain lived like that today" said the producer of the recent Central Television programmes. "Top level neglect is a thriving concern" and "community care may be on the tip of every fashionable tongue, but prison care is a likelier fate" according to a *BMJ* review. Daily papers and popular journals carried tragic case-histories. Dr Thomas Bewley, our President, had a supporting letter in *The Times*, and he and Professor Wing and other distinguished psychiatrists were at the crowded and eager seminar in Oxford organised by the National Schizophrenia Fellowship on March 17th.

Ignorance and prejudice about the disease are prevalent even among the educated. During the last week a woman has told me of her struggle to get her apparently schizophrenic son seen. The third GP advised her to throw the young man out, the fourth prescribed tranquillizers for her, but would not see the son. A general practitioner has told me that, in a lifetime's practice she had only seen one case of schizophrenia. Oxford academics have told me that they were not interested in schizophrenia as they did not have it in their colleges!

The National Schizophrenia Fellowship is an association of relatives and professionals to further the needs of sufferers and their families. We are concerned about the discharge of patients from mental hospitals to an uncaring community and the difficulty in getting admission for those in need of nursing and asylum. Ten times the present number of community psychiatric nurses need to be trained, social work training re-designed and satisfying occupation provided for the half million unemployable patients. Legislation is needed for treatment in the community of people who have lost insight in an acute episode. Psychiatric care for the mentally ill offender should be up to NHS standards.

As a result of close contact with sufferers, the NSF is convinced of the "medical model" for schizophrenia, and in the absence of a known cure acknowledges the need for drugs. We reject the view that schizophrenia is caused by faulty upbringing, psychiatric labelling or Western culture. Our organisation has extensive and specialised knowledge of schizophrenia which could and should be used in cooperation with the NHS for the benefit of sufferers and their families.

MARJORIE HARE

National Schizophrenia Fellowship
78 Victoria Road
Surbiton KT6 4NS

CORRECTION

(*Journal*, March 1986, **148,** 334). The second paragraph of the letter from Dr Sireling and Professor Paykel should read: "They suggest that the exclusion of patients who had seen a psychiatrist or received antidepressants in the past three months would have "creamed off" many severely depressed patients. We believe that antidepressants make patients less, not more severely depressed, and that the approximately 10% of depressed patients whom general practitioners refer to psychiatrists cannot be legitimately regarded as 'general practice depressives'."

British Journal of Psychiatry (1986), **148,** 617–623

Book Reviews

The Scientific Foundations of Psychiatry. Volume 5 of the **Handbook of Psychiatry.** Edited by Michael Shepherd. Cambridge: Cambridge University Press 1985. Pp. 359. £42.50 (hb), £17.50 (pb).

The completion of a textbook with strong claims to be foremost in its field is a superlative accomplishment calling for the widest recognition. Volume 5 concludes *The Handbook of Psychiatry* of which Michael Shepherd is the General Editor. The four parts of the volume deal in turn with: philosophy and psychiatry; epidemiology and genetics; social science, psychology and ethology; and, finally, the neurosciences. The last 66 pages are the Cumulative Index for all five volumes of the *Handbook*.

In the foreword, Shepherd stipulates the "Maudsley" approach to psychological medicine, emphasising that no merely British approach is implied. The origin of the approach was on the European continent, developed further in the United States with Adolf Meyer, and only then in the United Kingdom where Aubrey Lewis became its chief architect. The tradition is represented as an adherence to scientific enquiry in clinical and basic research, with the social and psychological contributions properly recognised, and the natural sciences also acknowledged.

This final volume presents reviews of the different scientific modes of enquiry on which psychiatry is founded, a large task. Not all scientific branches of knowledge are judged sufficiently established as yet to warrant inclusion (immunology and information science are examples). In the opening brief chapter on philosophy, sub-titled "some reflections on the nature of psychiatry", B. A. Farrell takes the view that psychiatric knowledge has eight components which need particular epistemological attention: 1. Classification of the phenomena of mental disorder, as organised in the post-Kraepelinian scheme; 2. Psycho-dynamic theories, the status of which is unsettled; 3. Organic pathology; 4. The criterial features of disorders (symptoms); 5. Non-criterial knowledge acquired through clinical experience and judgement, which cannot be codified strictly enough to satisfy standards of natural science; 6. Claims about treatment, which cannot be formulated in any one generally accepted way—there are differences of belief and emphasis among psychiatrists; 7. Predictions about the course of the different disorders: 8. The state of development of the sciences for investigation of how the brain functions; and 9. The relation that brain function has to personal and social aspects of human experience. Farrell, viewing psychiatry as still in a descriptive phase, insists that the psychiatrist will have to continue to rely on clinical judgement and experience for some centuries to come, and moreover will have to know how to apply the knowledge at his disposal for exercising clinical skill with an actual patient.

Norman Kreitman writing on epidemiology in Chapter 2 defines the basic terms with clarity and authority; he concludes with an instructive analysis of the complexity of "shared psychopathology"; epidemic suicide now appears to have been a major hazard in Roman legions stationed in remote areas; suicides of famous people have been shown to lead to a highly specific national pattern of imitation.

The chapter on genetics is brilliantly successful, written by a quintet of writers (including Irving Gottesman) supported by US grants, and notable for a multiplicity of definitions of both established and newly-formulated technical terms. The subject itself is divided into biochemical genetics, cytogenetics and population genetics, the last itself further subdivided into evolutionary genetics, genetic demography, biometrical genetics and genetic epidemiology. Both biological and behavioural aspects of the psychiatric genetics of disease are covered in Chapter 3.

The extent of overlap of the different sciences emerges early in the text. Kreitman emphasises how important elaborate statistical techniques are in epidemiology; the chapter on genetics refers to the recent development of concern with socio-cultural factors and with environmental factors (the latter either familial or non-familial). The sciences basic to psychiatry very evidently cannot be encapsulated. The recent work on the Wernicke-Korsakov syndrome is illustrative: only the 5% of alcoholics who are also thiamine-deficient appear to develop the syndrome. An inborn error of metabolism therefore seems to be implicated, but the indications are that it is clinically important only when dietary thiamine is also inadequate. The crucial place of multidisciplinarity is also emphasised in the conclusion of the chapter on genetics: productive research into psychiatric disorders will require close collaboration between genetic epidemiologists, neurobiologists, and clinicians. Mixed models for hypothesis-testing are now necessary, such as combined polygenic cultural models to explore biological and socio-cultural risk factors for multifactorial variation.

David Mechanic writes the chapter on social science, which provides concepts amd methods to study non-biological aspects of psychiatry. The key themes singled out from the social sciences are social cohesion, social stratification, sex, illness behaviour, helpseeking, societal reaction, labelling theory, attribution theory, the self, coping, and social effects on illness. Sociological concepts correct for the bias to regard behaviour and personality as largely inborn. Some of Mechanic's assertions unfortunately err drastically: "Clinical psychiatry is less concerned with defining the nature of illness than with developing useful interventions in instances of personal suffering or chronic bizzare and inappropriate functioning." Not to see that both responses are obligatory is a curious conceptual aberration.

Psychology (chapters 5 and 6) is represented by consideration of psychophysiology, biometrics, and also an area about which the editor has well-known reservations, the psychodynamic contribution (referred to in inverted commas in his Preface). Joseph Zubin is the senior author of the chapter on "general clinical" psychology. In it the term "phenomenology" is used to designate symptoms, signs and syndromes. This chapter concentrates on "those underpinnings of psychopathology" deriving from experimental psychology, particularly behavioural approaches based on quantitative methods. "In one sense, the biometric approach serves as a form of quality control for the field of psychopathology..." Biometrics is further designated as well as the conscience of psychiatry, through making techniques available for assessing its efficacy. The discussion of the clinical reasoning process by which a clinician makes diagnoses indicates only cursory knowledge about the extensive recent educational research in this area. The contributions deriving historically from England are conveyed in two short paragraphs, with sharp reference to falsification of data (by Burt, who is not mentioned by name).

The corresponding United States, contribution is accorded many pages. English recognition revives with a paragraph on Hans Eysenck. Consideration is given in the chapter to the biological and psychosocial models of disease as contrasted with the vulnerability model (and the role of life-event stressors). The chapter is wise, eminently competent in what it aims to convey, and admirable in its balance of particular illustrations with higher order generalizations which give form to the presentation.

Kräupl Taylor writes on dynamic psychology and Robert Hinde on ethology. Thus erudite attention is given to the "confusing proliferation of psychodynamic theories in conflict with each other", but the different "schools" are not accorded valid scope other than in their relation to classical psychoanalysis. Hinde iterates that conclusions drawn from studies of animals cannot be applied directly to the human case: indeed, it is often the differences from the human that make the animal case interesting. Neurophysiology has given rise to neuropharmacology and neurochemistry (dealt with in chapter 8) and neuroendocrinology (chapter 9). Crow and Deakin (chapter 8) conclude that the "neurohumoral hypothesis" has greatly elucidated the mechanism of action of psychotropic drugs and encouraged the belief that "it may be possible to understand psychiatric disease... in terms of specific disturbances of neuro-transmitter function." They end with the theory that some psychiatric diseases result from a specific chemical interaction between a virus and a neuronal cell surface component (e.g. a neurotransmitter receptor).

Donovan reviews neuroendocrinology, and cites Beach's (1975) report that bitches masculinised by exposure to testosterone *in utero* do not squat to urinate but raise a hind leg, and manifest male mounting behaviour only after additional treatment with androgen. However, Kinsey's view appears vindicated as a generalisation, that once the period of sexual differentiation and development is past, there are no specific effects of gonadal hormones upon human sexual behaviour. The importance of hormones in determining gender identity still remains debatable; there is no persuasive evidence for any hormonal difference in homosexuality.

Neuropathology, dealt with by Corsellis and Janota, has not yet yielded any clearly defined process or abnormality as the substrate for the functional psychiatric disorders, schizophrenia particularly. "So often the initial burst of enthusiasm for some pathological revelation has gradually withered away..." They conclude it is impossible to know whether schizophrenia has an organic basis or even an organic element.

An editor or other writer expects commentators to give gratuitous advice (the term "Kibitzer" from the Yiddish designates them), and to point out various areas of neglect, hopefully to receive attention in later editions. It is remarkable in a book which is about science after all, for the status of knowledge itself to get little attention—other than Farrell's general remarks. This is a time of revolutions and reconstructions in the philosophy of science, as Mary Hesse (1984, Harvester Press) emphasises in the title she chose for her recent book on the subject. The editor may well want to reflect in the next edition that the science of science is now in a post-empiricist phase, when values are given special attention—of the greatest relevance to psychiatry, a value-laden subject if ever there was one.

Next, while Kräupl Taylor is one of the most sensible writers alive on the subject of psychodynamics, his limited consideration of the inner world of man, "lived experience", simply will not do as sufficient treatment of subjectivity in psychiatry. In any claim to that effect the *Handbook* reduces psychiatry itself and pulls the shutters down in many mansions of the house that Kraepelin built, because he certainly was a true clinician as well as a scientist.

The other omission, remarkable for an avowed Jasperian, is the field of phenomenology proper. The name of Husserl only appears on p. 109, and Heidegger is cited once in passing on p. 113, without a comment about his large influence on psychiatry. The notion that phenomenology has any claim to be regarded as a basic scientific method in clinical psychiatry is not mentioned, even in repudiation.

This concluding volume on the sciences basic to psychiatry admirably brings the vast enterprise to a close, calling on the collaboration of a sizeable cohort of writers who have been commendably selected, marshalled and organised. The *Handbook* is worthy to stand beside its no less substantial but strikingly different companion work, the *Comprehensive Textbook of Psychiatry* edited by Kaplan, Freedman and Sadock. Psychiatrists are privileged to have two great compilations, one admirably complementing the other, and for optimal coverage will want to have both.

HENRY J. WALTON, *Professor of Psychiatry, Royal Edinburgh Hospital, Edinburgh*

Freud for Historians. By Peter Gay. Oxford University Press: New York & Oxford. 1986. Pp. 252. £16.50.

George Steiner has commented on the Holocaust that "Where history went mad, the inventorising of facts is not enough"; professional historians, having said *what* had happened, they ought at least to speculate as to *why* this had been so. At present they are ill-equiped for the task. Looking for a helpful theory or framework, they could well be tempted towards psycho-analysis—perhaps the ultimate source of retrospective explanations, though not of predictions. It has already produced those techniques of dubious legitimacy—psycho-biography and psycho-history—but are the answers to the riddles of human motivation really to be found in what Peter Gay himself calls those "much canvassed disasters"?

He is a distinguished historian who saw a vision (of Freud) on the road (to New Haven, Connecticut), causing him to qualify in mid-career as a psycho-analyst, and all the fervour of a proselyte can be seen in his wish that others should share this enlightment. For him, psycho-analysts and historians are allies in the struggle against "naive and crude monocausal explanations", and their collaboration might allow a firm grasp on the totality of human experience. But at the same time as looking for a new psychological basis to the science/art of history, Professor Gay has been writing a major study of nineteenth century bourgeois culture from a psycho-analytical prospective. No sluggard he.

Clearly enough, motivation has never been totally ignored by the professional historian, who is inevitably "a psychologist—an amateur one". Though historians are uncomfortable with the idea of human nature, they must still operate with a theory of it—"but much of the operation is secret—even to them"; they are not most at home with the unruly mass of impulses and ideas lying beneath the surface of human consiousness. Yet the proper use of psycho-analytical concepts could "take us away from obscure or abstract speculation into the heart of psychological dynamics", and provide an informed style of inquiry, supplying answers no-one had thought were available or even suggesting questions no-one had thought to ask. For instance, every political upheaval has polarised people so that they have idealised one side and execrated the other; psycho-analysis explains this as a "splitting" which retreats from more adult modes of perceiving the world. The presence or absence or irrational excitement, or the size of the gap between actual and rationally necessary expenditures of energy are not very exact measures, but Gay says they are "as precise and telling as anything can be in a psychology working with mental materials that really matter".

If that doesn't sound very objective to psychiatrists, the author could challenge them to show him a view of history which did; some might suggest Marxism, but that version of "objectivity" seems to mean conformity to an individual's vision which was no less subjective than Freud's. On the other hand, Gay's claim that the fundaments of Freud's theoretical structure "have received some impressive experimental support" is unconvincing, and when he adds that "The discovery just how deeply private emotions are invested in public life is only one way in which Freud's theories can move history beyond sheer biography", more precision is needed in his use of "discovery".

But to return to the Holocaust, Professor Gay is perhaps on firmer ground in suggesting that "collective irrationality" seems to be the proper province for the psycho-analysts' specialised competence, and that the Freudian historian tends to be seen as the expert of last resort when rational causes are not found for outbursts of bigotry or self-destructive behaviour. If self-interest should be offered as the motivation for most human actions, he replies that "historians have rarely troubled to analyse its psychological status or to trace its actual incidence in human life"; should they do so now, psycho-analysis could help them to detect and disarm their prejudices.

Or will it merely give them a new set? As always, this author's display of scholarship and verbal pyrotechnics tends to sweep all before it, but he does not confront the practical question of how historians in general might acquire enough knowledge of Freudian theory to gain the kinds of insight he claims for it. Yet if they had less than that, would such a smattering make them better historians?

HUGH FREEMAN, *Consultant Psychiatrist, Hope Hospital, Salford*

Freud: An Introduction to His Life and Work. By J. N. Isbister. Oxford: Polity Press. 1985. Pp. 318. £25.00 (hb), £6.95 (pb).

For many years, the standard account of Freud's life and work was the 3-volume biography by Ernest Jones. It had a number of virtues. It was written by a man who had a long association with Freud, who knew the Freud family over many years, and who was thoroughly familiar with psychoanalysis and its subject matter. It was beautifully written (W. H. Auden called it a "masterpiece"). It was put together with meticulous care and was the work of a major intelligence. It was undoubtedly a labour of love. This may have led, at times, to a note of idealisation which was by no means intrusive but which is sometimes seized on with eagerness by those who are busy re-writing early psychoanalytic history.

It is both right and inevitable that later biographers seek to uncover new facts and to throw further light on creative thinkers who continue to have a major influence on our time. But what commands the attention of a present-day observer is the continuing stream of publications which make a virtue of ambivalence in the apparent belief that this fosters a balanced view. For writers of this kind, Jones's commitment is suspect indeed.

Books which are plainly hostile declare their authors' position and, on account of their openness, are unlikely to mislead those who seek an informed understanding of Freudian psychoanalysis. Their appeal to the prejudiced is after all harmless. Much more insidious are those "balanced" presentations that discuss Freud with an appearance of scholarship but which lack real intellectual rigour.

It has to be said that Dr Isbister's book comes into this category. The numerous quotations, notes, and references may all too easily persuade the uninformed reader that this is a work of authority. The fact is that a number of references on which some of the author's more dubious arguments depend are to mere assertions or unfounded speculations. It is unfortunate that, when material of this kind is intermingled with much more accurate and well-supported statements, the result is all the more misleading for the unwary. And it simply will not do to write a biography of Freud which attaches so much importance to such fanciful notions as Freud's supposed but quite improbable affair with Minna Bernays. It may be argued that, while this does not speak well for the author's priority, it is otherwise of no great importance. But it is. It is one of the ways in which Freud can be portrayed as deceitful and hypocritical; and Dr Isbister is not alone in using such methods to cast doubt on Freud's probity. That distinguished philosopher, the late Walter Kaufmann, has shown very vividly and compellingly how a man's work may be made to appear vulnerable or even vitiated by impugning his character. Those who want to understand the influence of Freud's character on his studies of the mind cannot do better than consult Kaufmann's book *Discovering the Mind* (1980).

This may be one reason why, as an exposition of Freud's work, Dr Isbister's account fails in its intention to provide a really useful introduction. But it does not explain the idiosyncracy of the presentation. The disproportionate space given to Freud's early and pre-analytic writings does little to help the newcomer, while its unsatisfactory nature may reflect the influence of Peter Swailes. I find it difficult to understand how anyone who has clearly devoted innumerable hours to the subject should manage to produce an account of psychoanalysis which shows such an inadequate grasp of its basic concepts. Perhaps Dr Isbister's book exemplifies the fact that it is possible to read and assimilate widely, but without understanding.

One last comment. One of the books to which Dr

Isbister directs his readers is the so-called *Cocaine Papers* (1974), edited by Byck, with purported "notes by Anna Freud". Anna Freud was highly indignant when she first saw a copy of this book about which she said she had never been consulted, and which contains supposed quotations from her on subjects about which she said she knew nothing and which she had never written. This may be a forgiveable error on Dr Isbister's part; but it is certainly not the only solecism which calls the author's scholarship into question.

CLIFFORD YORKE, *Formerly Consultant in Mental Health (Psychotherapy), Watford General Hospital*

Foundations of Aversion Therapy. By NORMAN H. HADLEY. Lancaster: MTP Press. 1985. Pp. 145. £24.95.

I commenced reading this book with curiosity, wondering if I had overlooked some recent advances in the clinical use of aversion therapy. Generally, I considered aversion techniques to be outdated and unpleasant forms of treatment surrounded by multiple moral and ethical problems and of little use except in rare life threatening or other dangerous situations. After reading the book my view was unchanged.

The book describes the basic principles of conditioning, learning theory and aspects of current experimental psychology research which have relevance to aversion therapy. There are few references to clinical practice and, for example, although faradic aversion and facial screening procedures are described in some detail, guidelines on the specific clinical situations where they may have a role in treatment are missing.

I was also unconvinced of the applicability of this book for most professionals in Britain. In the preface, the author states it is written "for students of graduate and advanced graduate courses in behaviour therapy and for the applied researcher or clinician in aversion behaviour therapy." However, I feel that it would be of little interest to clinicians of all disciplines due to the lack of practical clinical advice. Although it covers relevant areas of experimental psychology, it is too basic to be of interest to researchers or students of psychology. Nevertheless, the book is concise and well illustrated with clear diagrams. I found it a useful revision of learning theory. My reticence in recommending it lies in its lack of relevance to modern behaviour therapy.

LYNNE M. DRUMMOND, *Senior Lecturer in Behavioural Psychotherapy, St George's Hospital Medical School, London*

Children with Emotional Disorders and Developmental Disabilities: Assessment and Treatment. Edited by MARIAN SIGMAN. Orlando, Florida: Grune & Stratton. 1985. Pp 346. $34.50.

The title of this book does not really indicate what it is about. In fact, it is concerned with mental handicap, particularly in childhood and adolescence, when psychiatric disorder happens to be associated, as of course it often is. It is written by about twenty PhDs and a couple of MDs, approximately half of whom work at the University of California, Los Angeles. The first section provides an informative account of the development of personal relationships, emotional expression, language and social adjustment in the intellectually retarded. Next comes several chapters on psychiatric disorders associated with low IQ, including autism. Related problems of adult life are also dealt with to some extent. The third and last section of the book is concerned with assessment and treatment. Psychological testing and psychiatric diagnosis are covered. Appropriate educational facilities, behavioural approaches, psychotherapy and family therapy are included.

The book maintains a uniformly high standard throughout. It covers relevant literature and provides a good source of references to recent work. Mary O'Connor's chapter on cognitive assessment is a remarkably clear and practical account of testing retarded children. Unfortunately for British readers, some scales used in this country have not been included. The contribution on the diagnosis of mental disorders by Ludwik Szymanoki from the Children's Hospital Medical Centre, Boston, is inadequate by United Kingdom standards.

All those who work with mentally handicapped children and their families, which includes most child and adolescent psychiatrists, will find something of interest in this book.

IAN BERG, *Consultant in Child and Adolescent Psychiatry, Leeds General Infirmary*

Behavioral Theories and Treatment of Anxiety. Edited by SAMUEL M. TURNER. New York: Plenum. 1984. Pp 437. $45.00.

In recent years, there has been a dearth of major text books on traditional behavioural techniques, presumably as a result of an increased interest in the related field of cognitive therapy. To those who are confused as to the reformulated theoretical model underlying this approach, or who are unsure of the relative merits of, say flooding and self-statement training, this volume will be seen as a welcome addition to the literature. The authors have conducted a thorough survey of the most recent empirical evidence and the conclusions reached may well cause academics and clinicians alike to revise their opinions regarding the status of paradigms and procedures which have come to be regarded as outmoded.

The format of the book is relatively straightforward, with each chapter being devoted to a particular neurotic disorder. In addition to such predictable topics as simple phobias, agoraphobia, and obsessive-compulsive neurosis, the editor has chosen to include two interesting papers on childhood anxiety disorders, which are all too rarely covered in depth in texts of this kind. However, perhaps the most innovative chapter is that on social phobia which, incidentally, is the sole contribution by British authors to this volume. Trower and Turland offer an extremely sophisticated model of interpersonal difficulties, derived from social learning theory, which has important implications for assessment and treatment.

This book is extremely well-edited with each of the authors working within strict guidelines which have clearly been laid down for them. This has the advantage of enabling the reader to quickly evaluate the status of a particular technique in relation to a wide variety of disorders. The bibliography is extensive and the quality of presentation is consistently high. Given the current scarcity of up-to-date reviews of the behaviour therapy literature, this volume can be strongly recommended to all those involved in applying this approach with anxiety related disorders. In addition it will be read with considerable interest by postgraduate students who are undergoing further training in psychiatry.

DOUGAL MACKAY, *District Psychologist, Bristol and Weston Health Authority, Barrow Hospital, Bristol*

The Psychology of Religion. By JOSEPH F. BYRNES. New York: The Free Press. 1984. Pp. 308. $24.95.

This book is a synthesis of the possibilities and limitations of considering the relationship of psychology to religion. The author has expounded a variety of psychological constructs, ranging through the analytical, behavioural and existential schools, laying special stress on those areas in each which seem to bear on religious experience. He shows how each theory might approach the mystical experience, the conversion experience and religious behaviour. He concludes the work by an examination of a number of research projects which have examined forms of religious experience.

The study offers a number of differing ways in which people may have a false or skewed basis to their religious experience and, as such, helps to avoid any single attitude towards such experience. This can be of value to any therapist who finds that his own theoretical construct does not fit the situation.

On the other hand the very fact that he is able to show that religious experience can be fitted into almost any construct may make one wonder how far the facts have been made to fit the particular theory. It is interesting to note that he does not quote any of the letters between Freud and Pfister which demonstrate Freud's real feelings in the matter. The research is all taken from the USA and does not take into account that which was done by Heije Faber (*Psychology of Religion*: SCM, 1972) or by Irene Bloomfield and myself (*Psychosexual Problems*, ed. S. Crown: Academic Press, 1976) which do not accord with many of his conclusions.

LOUIS MARTEAU, *Dympna Centre, London*

Childhood Disorders: Behavioural-Developmental Approaches. Edited by ROBERT J. MCMAHON and RAY DEV. PETERS. New York: Brunner/Mazwel. 1985. Pp. 274. £39.00.

This book is a collection of papers by those who attended the 1983 Banff International Conference on Behavioural Sciences. Three chapters are concerned with conceptual foundations: the integration of behaviour and developmental approaches to childhood disorders, applied behaviour analysis, and the cognitive: behavioural perspective. These are followed by eight chapters on assessment and treatment. The two on assessment are by Achenbach on taxonomy and taxometry and Bricker and Littman on a parental questionnaire to monitor infant development. The remaining chapters are concerned with intervention namely: the integration of exceptional children and handicapped children under "normal" environments, childhood autism, child abuse, hyperactive children, and parent/adolescent conflicts.

The authors are predominantly psychologists who understandably emphasise their perspective and potential contribution to the assessment and treatment of childhood disorders. The predominant format is reviews although some chapters include data from one or more studies. Initially, a rather unhelpful polemical chapter on behavioural analysis is sandwiched between a sensible statement about the need to integrate developmental considerations into clinical psychology and a balanced review of cognitive-behavioural perspectives. Almost all the subsequent chapters have nothing of interest although the extent of this will depend on individual readers. Whether the parental monitoring questionnaire of infant development will prove useful will depend on further studies. Although the results of the social skills training programme to integrate handicapped children were modest it appears promising. Some will find the chapter on the prevention of child abuse optimistic. The chapter on parent/ adolescent conflict outlines a very didactic approach to family therapy which, as the author himself comments, raises the question of which families would benefit mostly from which components of the intervention.

Overall this is a worthwhile group of reviews, although it has to be said that most of the material is available elsewhere.

A. D. COX, *Senior Lecturer in Child and Adolescent Psychiatry, Institute of Psychiatry, London*

The Long-Term Treatment of Functional Psychoses: Needed Areas of Research. Edited by T. HELGASON. Cambridge: Cambridge University Press. 1985. Pp 270. £30.00.

This is the report of a workshop held in Italy in 1983. It was organised by a body known as the Study Group on Mental Illness Research of the European Medical Research Councils. Its official aim is to exchange information on research activities between the main European countries. One of the contributors described the purpose of the volume as "rather than looking for the right answers, to find some relevant questions for further research in the puzzling field of functional psychoses". Certainly most of the 26 chapters contain ideas for research and in this sense the volume might be useful in suggesting topics to a young psychiatrist with a desire to carry out research but with no clear direction.

There are contributions from Leff, Wing, Priest and

Goldberg from Britain and the rest are mainly from Germany, Switzerland and Scandinavia. The emphasis is on psychosocial treatment of psychosis rather than biological, and such matters are not easily tackled by a young, lone researcher. Many of the suggested topics for further research are clearly aimed at governments or at least wealthy institutions, e.g. "we are in need of comprehensive longitudinal studies of the whole rehabilitation process". For this reason I doubt if any of the questions will in fact stimulate a keen young mind.

In Britain in the 1980s there is a swing away from psychosocial formulations of schizophrenia. Perhaps the advent of CT scanning was responsible. Perhaps the psychosocial questions were too vague or too general; this is certainly the case with many of these in this book.

J. CUTTING, *Consultant Psychiatrist, The Bethlem Royal Hospital, Beckenham, Kent*

Antipsychotics (Drugs in Psychiatry, Volume 3). Edited by GRAHAM D. BURROWS, TREVOR R. NORMAN and BRIAN DAVIES. Amsterdam: Elsevier. 1985. Pp 279. $72.25. Dfl. 195.00.

This book is the third in the *Drugs in Psychiatry* series and maintains their usual high standard. There is a section on basic research covering the neuroendocrine effects and prediction of response of antipsychotic drugs, and antipsychotic actions of endorphins. The section on plasma level measurement, pharmacokinetics and clinical response includes chapters on phenothiazines, butyrophenones, thioxanthines, clozapine and loxapine. The section on clinical applications covers new antipsychotic agents, benzodiazepines, long-acting neuroleptic drugs, tardive dyskinesia, neuroleptics in children and the elderly, and the adverse effects and drug interactions of antipsychotics.

The reviews are generally comprehensive and up-to-date. The book appears directed to experienced clinicians, stressing psychopharmacology and pharmacokinetics. There is emphasis on new frontiers of antipsychotic therapy. I found the chapter on tardive dyskinesia to be especially enjoyable and rewarding to read.

On the other hand, the book might be less useful to trainees in psychiatry, as there is relatively little discussion of clinical syndromes, the interaction of medication with psychological and social therapies or the practical management problems facing general clinical psychiatrists. Nevertheless, this book presents the psychopharmacology of antipsychotics in a clear and concise fashion. At a price of $72.25, it is more likely to be bought by libraries and psychopharmacologists than by general psychiatrists or trainees.

MICHAEL A. REVELEY, *Senior Lecturer in Psychiatry, London Hospital Medical College, London*

Multiple Choice Questions in Psychiatry. By JAMES MAGUIRE, PATRICK MCKEON and KIERAN POWER. London: Pitman. 1985. Pp 140. £5.95.

This book offers two hundred questions of the multiple true-false type drawn from a wide range of psychiatric topics. The order of the questions is random but an index can direct the reader to the relevant questions for any given subject. The coverage is arguably unbalanced. While forensic psychiatry warrants twenty questions only three are devoted to psychogeriatrics.

There is now little excuse for MCQ books which do not provide adequate explanations for their answers, so I was pleased to discover the brief but useful explanations substantiating this book's answers as well as supplying some additional information. References are given, usually to review articles or readily available textbooks.

The questions are generally of appropriate difficulty for those approaching the MRCPsych II examination. Some topics such as genetics, epidemiology and phenomenology are clearly relevant to the preliminary test. Certain questions would be suitable for medical students.

Although the questions are generally well-composed some difficulties in MCQ writing are occasionally illustrated. For instance, words conveying undue certainty such as "never", "always", "only", "invariably", "unique", "conclusive" tend to be giveaways in the indefinite world of psychiatry to all but the most naive MCQ respondents. Again, words like "common" or "rare" can be problematical. How common is common? One explanation says visual hallucinations are uncommon in schizophrenia. Minor reservations apart, this is a book which should inform as well as allow self-assessment and I recommend it.

ROGER FARMER, *Lecturer in Psychiatry, St Mary's Hospital, London*

THE AMERICAN JOURNAL OF PSYCHIATRY

Volume 143, Number 4 **April 1986**

Special Article

417 Psychological and Social Aspects of the Surgical Treatment of Obesity *Albert J. Stunkard, James L. Stinnett and Jordon W. Smoller*
430 Psychotherapy of the Narcissistic Personality Disorder Patient: Two Contrasting Approaches *Gerald Adler*

Regular Articles

437 The Prognostic Significance of Obsessive-Compulsive Symptoms in Schizophrenia *Wayne S. Fenton and Thomas H. McGlashan*
442 Cortisol and Alzheimer's Disease, II: Dexamethasone Suppression, Dementia Severity, and Affective Symptoms *Blaine S. Greenwald, Aleksander A. Mathe, Richard C. Mohs, Michael I. Levy, Celeste A. Johns and Kenneth L. Davis*
447 Depression in Women Treated for Gynecological Cancer: Clinical and Neuroendocrine Assessment *Dwight Landis Evans, Cheryl F. McCartney, Charles B. Nemeroff, David Raft, Dana Quade, Robert N. Golden, John J. Haggerty Jr, Valerie Holmes, Jeffrey S. Simon, Marion Droba, George A. Mason, Wesley D. Fowler*
452 Dexamethasone Suppression in Dementia, Depression and Normal Aging *Anastasios Georgotas, Robert E. McCue, O. Mary Kim, William E. Hapworth, Barry Reisberg, Peter M. Stoll, Elia Sinaiko, Christine Fanelli and Peter E. Stokes*
457 Lithium Ion Transport by Erythrocytes of Randomly Selected Blood Donors and Manic-Depressive Patients: Lack of Association With Affective Illness *Elliott Richelson, Karen Snyder, John Carlson, Mark Johnson, Stephen Turner, Ann Lumry, Eric Boerwinkle, Charles F. Sing*
463 Proposed Changes in *DSM-III* Substance Use Disorders: Description and Rationale *Bruce J. Rounsaville, Robert L. Spitzer and Janet B. W. Williams*

Special Section

469 The Application of Postiron Emission Tomography to the Study of Panic Disorder *Eric M. Reiman, Marcus E. Raichle, Eli Robins, F. Kevin Butler, Peter Herscovitch, Peter Fox and Joel Perlmutter*
478 Ambulatory Heart Rate Changes in Patients With Panic Attacks *C. Barr Taylor, Jevald Sheikh, W. Stewart Agras, Walton T. Roth, Juergen Margraf, Anke Ehlers, Richard J. Maddock and Denis Gossard*
483 Neuroendocrine Correlates of Lactate-Induced Anxiety and Their Response to Chronic Alprazolam Therapy *Daniel B. Carr, David V. Sheehan, Owen S. Surman, James H. Coleman, David J. Greenblatt, George R. Heninger, Kenneth J. Jones, Peter H. Levine and W. David Watkins*
495 Possible Mechanisms for Lactate's Induction of Panic *Michael R. Liebowitz, Jack M. Gorman, Abby Fyer, Donald Dillon, Morton Levitt and Donald F. Klein*
503 Reduced TSH and Prolactin Responses to TRH in Patients With Panic Disorder *Peter P. Roy-Byrne, Thomas W. Uhde, David R. Rubinow and Robert M. Post*
508 Mortality Among Outpatients with Anxiety Disorders *William Coryell, Russell Noyes Jr, and Daniel J. House*
511 The Prevalence of Mitral Valve Prolapse in Patients With Panic Disorders *Richard Liberthson, David V. Sheehan, Mary Etta King and Arthur E. Weyman*

Editorial

516 Biological Aspects of Panic Disorder *James C. Ballenger*

Brief Communications

519 Positive Effects of Carbamazepine on Behavioural Dyscontrol in Borderline Personality Disorder *David L. Gardner and Rex W. Cowdry*
523 Social Skill Training for Schizophrenic Individuals at Risk for Relapse *Robert Paul Liberman, Kim T. Musser and Charles J. Wallace*
527 Phenomenological Comparison of Poststroke Depression and Functional Depression *John R. Lipsey, Wendy C. Spencer, Peter V. Rabins, Robert G. Robinson*
530 Concomitant Obsessive-Compulsive Disorder and Schizotypal Personality Disorder *Michael A. Jenike, Lee Baer, William E. Minichiello, Carl E. Schwartz and Robert J. Carey Jr*

Clinical and Research Reports

533 Differentiation of Anxious Patients by Two-Dimensional Echocardiographic Evaluation of the Mitral Valve *Stephen R. Dager, Keith A. Comess and David L. Dunner*
535 Neuroleptic Dosage for Asians: A Failure to Replicate *John J. Sramek, Marsha A. Sayles and George M. Simpson*
537 Measurement of Combat Exposure, Posttraumatic Stress Disorder and Life Stress Among Vietnam Combat Veterans *Matthew J. Friedman, Carla K. Schneiderman, Alan N. West and John A. Corson*
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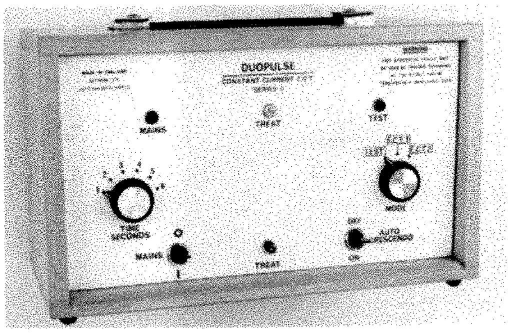

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Index to Advertisers

Pharmaceuticals

The Boots Company plc	*facing* p 517
Brocades GB Limited	p ii
CP Pharmaceuticals Limited	p viii
Geigy Pharmaceuticals	*facing* p 540
Janssen Pharmaceutical Limited	*facing* p 540
May & Baker Limited	*facing* p 516
E. Merck Limited	*facing* p 541
E. R. Squibb & Sons Limited	*facing* p 532 and 533

Booksellers and Publishers

Associated Book Publishers (Tavistock)	p iii
William Heinemann Medical Books Ltd	p iii

Clinics, Hospitals and Nursing Homes

Bowden House Clinic	p v
Charter Clinic	p vii
Ticehurst House Hospital	p iii
The Retreat	*inside back cover*

Appointments

Illawarra Area Health Service	p iv
Malawi High Commission	p iv
University of Otago	p ii

Miscellaneous

Holwell Centre for Psychodrama	p ii
International Conference on Mental Health & Technology	p vi
The Queen's University of Belfast	p ii

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THE BRITISH JOURNAL OF PSYCHIATRY

May 1986 Volume 148

Annotation

Treatment of Prolonged Combat Reaction; *A. Bleich, R. Garb and M. Kottler* 493

Lecture

Mindlessness and Brainlessness in Psychiatry; *Leon Eisenberg* 497

Papers

Deficits of Chronic Schizophrenia in Relation to Long-Term Hospitalisation; *P. John Mathai and P. S. Gopinath* 509
Clinical Tests of Memory; *Michael D. Kopelman* 517
Respiratory Control in the Treatment of Panic Attacks: Replication and Extension with Concurrent Measurement of Behaviour and pCO_2; *Paul M. Salkovskis, David R. O. Jones and David M. Clark* 526
At Risk Drinking among General Practice Attenders: Prevalence, Characteristics and Alcohol-Related Problems; *Michael King* 533
Depression Influences Intellectual Impairment in Stroke Patients; *Robert G. Robinson, Karen Bolla-Wilson, Edith Kaplan, John R. Lipsey and Thomas R. Price* 541
The Validation of the GHQ-28 and the use of the MMSE in Neurological In-Patients; *Keith W. Bridges and David P. Goldberg* 548
Depression, Hopelessness and Suicide in Chronic Schizophrenia; *Robert E. Drake and Paul G. Cotton* 554
Pharmacokinetics and Therapeutic Efficacy of Haloperidol Decanoate after Loading Dose Administration; *H. De Cuyper, J. Bollen, H. M. van Praag and D. Verstraeten* 560
A Multivariate Investigation of Postpartum Mood Disturbance; *P. R. Gard, S. L. Handley, A. D. Parsons and G. Waldron* 567
The Prevalence of Schizophrenia in a Remote Area of Botswana; *David I. Ben-Tovim and Josephine M. Cushnie* 576
Development of Scales to Measure Treatment Attitudes in Psychiatry; *Greg Wilkinson and Paul Williams* 581

Comment

Positive and Negative Symptoms in Psychiatry; *Michael R. Trimble* 587

Brief Reports

Comparative Effects of Seven Antidepressant Regimes on Appetite, Weight and Carbohydrate Preference; *Brian Harris, John Young and Bill Hughes* 590
Schneiderian First Rank Symptoms caused by Benzodiazepine Withdrawal; *Keith Roberts and Neil Vass* 593
Manic Depressive Psychosis in a Mentally Handicapped Person – Diagnosis and Management; *S. R. Kadambari* 595
Does Viloxazine Really Improve Sex Drive? A Double-Blind Controlled Study; *Diego De Leo and Guido Magni* 597
Grade Scores of the Montgomery-Åsberg Depression and the Clinical Anxiety Scales; *R. P. Snaith, F. M. Harrop, D. A. Newby and C. Teale* 599
Gilles de la Tourette's Syndrome in Down's Syndrome – A Case Report; *H. Karlinsky, P. Sandor, J. M. Berg, H. Moldofsky and E. Crawford* 601
Minimal Sedation Required with Nitrous Oxide-Oxygen Treatment of the Alcohol Withdrawal State; *M. A. Gillman and F. J. Lichtigfeld* 604
One Hundred Cases of Hysteria in Eastern Libya: A Socio-Demographic Study; *Tinnyunt Pu, E. Mohamed, Kareema Imam and Ali M. El-Roey* 606
Correspondence 610
Book Reviews 617

Notice to contributors, subscribers and advertisers inside front cover

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THE BRITISH JOURNAL OF PSYCHIATRY

June 1986 Vol 148

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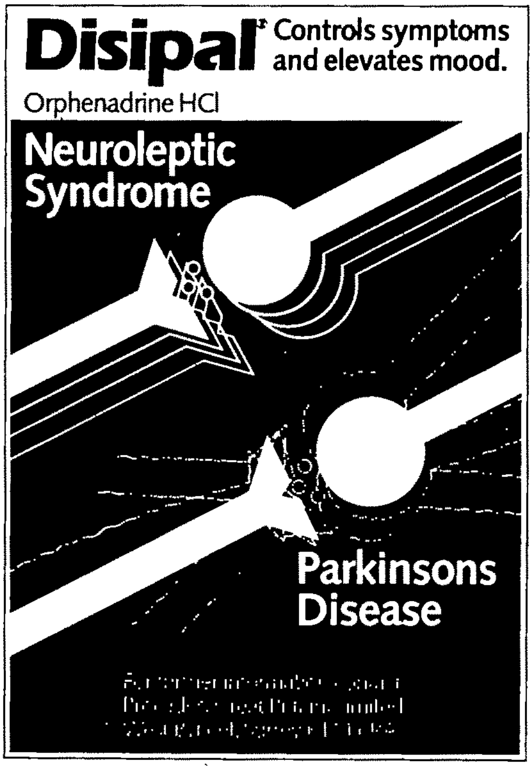

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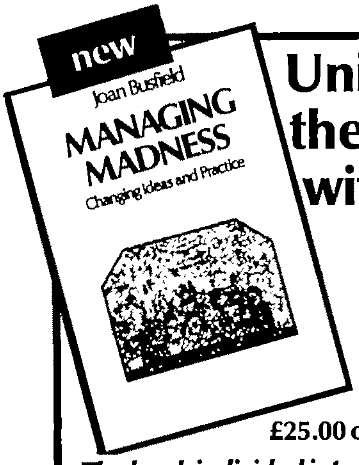

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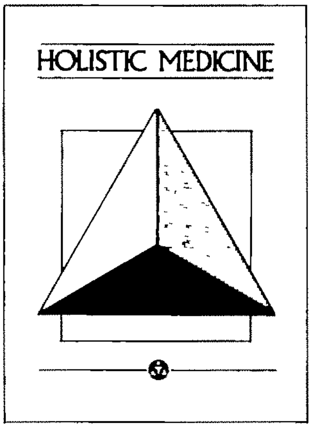

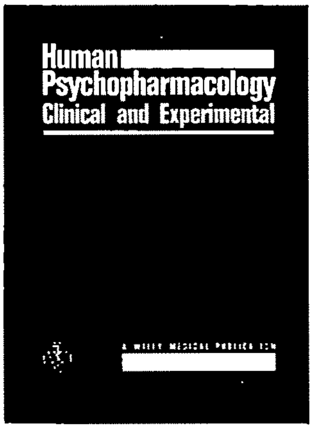

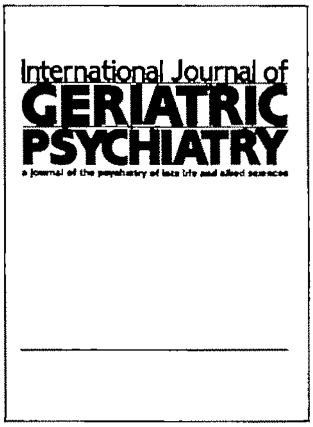
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Annotation

Dominance Hierarchies in Psychotherapy Groups

JAMES L. KENNEDY and K. ROY MACKENZIE

For a social group to develop, two opposing adaptive processes must be reconciled—mechanisms for developing cohesion and mechanisms for establishing a dominance hierarchy. The formation of stable groups provides significant evolutionary advantages: a source of protection, increased reproductive opportunities, and a larger store of survival strategies than any one individual could encompass. A recent theory of human evolution (Reynolds, 1981) stresses that social behaviour would seem to be the most likely single cause of the origin of human intelligence, if one origin must be isolated. Current interest in the biological basis of behaviour has been focused particularly on specific diagnostic categories and biochemical mechanisms. This paper reviews a different research tradition, based on ethological principles, and applies the findings to an understanding of human group behaviour.

Two quite separate fields of investigation will be reviewed. The first focuses on principles and mechanisms related to the establishment of a dominance hierarchy in primates and humans. The second deals with the stages a group must master to develop organisational complexity and stability. We are proposing that an understanding of the mechanisms of dominance formation illuminates our understanding of the phenomena of group stages, and may be of relevance to clinical practice. Innate tendencies in human behaviour arising from our evolutionary past may function to inhibit or facilitate the operation of therapeutic factors in group psychotherapy, while ethological studies help to identify the functional significance of aspects of human social behaviour. Few studies to date, however, have examined human group phenomena from an ethological perspective.

Formation of Dominance Hierarchies

Ethological field studies of primate species such as the rhesus, baboon, gorilla, chimpanzee and human document a variety of similar behavioural repertoires. These include the creation of a dominance hierarchy, aggression, grooming, and pair bonding. The dominance hierarchy consists of a ranking of members according to their power and influence in the group; ranking contests are customarily resolved through use of threat stares and postures. These rank order contests may become fierce, but rarely is a group member seriously injured (Eibl-Eibesfeldt, 1975).

The dominant member of a non-human primate group is usually the male who has the best combination of maturity and physical vigour; he generally determines the direction of group activity. He has a well-developed threat display, yet is able to balance this aggressiveness with the ability to form cooperative alliances with other members. The low-ranking member tends to avoid the dominant animal; he may turn away from the dominant animal's stare, display a characteristic 'appeasement grin', and adopt a crouching posture.

The phenomenon of dominance hierarchy formation has been repeatedly demonstrated in both male and female non-human primates. However, males appear to be more reactive to this interactional process, while female dominance rankings are more stable over time. When an animal is removed and then reintroduced to a group, females tend to settle into their original position in the dominance hierarchy, while males seldom do so, and indeed are often rejected by the group. Introduction of a strange animal elicits a stronger ranking response from males than females. Thus, while dominance effects are found across sex lines, females tend to have a less reactive response and a more stable hierarchy formation (Hausfater, 1975).

Dominance hierarchies in human groups have come under careful study only recently, but that children, most conspicuously boys, rank-order themselves is largely agreed. McGrew (1972) studied newly formed groups of nursery school children aged three to five years, and found evidence compatible with heirarchy formation: "aggression was absent at the outset, the children reacting to the situation with 'nervous caution'. As time went by aggression grew . . . the children seemed to be seeing how far a quarrel could be pushed until tears resulted". Weisfeld *et al* (1980) concluded that human males negotiate a critical or sensitive period from about four to seven years of age, during which their position in the dominance hierarchy becomes established; longitudinal assessment of subsequent development of these children led to the conclusion that the outcome of these emergent dominance struggles will predictably affect social interactions through adolescence and possibly beyond. Barkow (1980) states that "the agonistic aspect of social ranking in young children is remarkably similar to non-human primates. As the child matures, he increasingly comes to supplement the primate agonistic hierarchy with one based on culturally constituted, symbolic criteria for the evaluation of relative standing". The same author suggests that there is a regression to rank determination based on physical size and agonistic factors in times of stress or when verbal communication is blocked.

The application of ethological principles to psychiatry is relatively new (McGuire & Fairbanks, 1977), but research on human behaviour in psychotherapy groups is providing a set of data which is amenable to comparison with ethological studies of other species. Buirski *et al* (1978) found in a series of studies that measures of dominance rank made by the members of psychotherapy groups were similar to the group leader's estimate of rank in short term process groups, suggesting the reliability of the rank-order measure. Using the Emotions Profile Index (EPI), these authors report a strong correlation between certain emotional characteristics of individuals and their position in the hierarchy. High ranking members tended to be the 'most liked' members of the group, to have a greater feeling of 'joy', to exhibit more 'expressed control' and in some cases to be more aggressive. Low-ranking individuals showed significantly higher scores in the characteristics of 'fear', 'timidity', 'expectancy', and 'impulsivity'. Females tended to predominate in lower ranks.

Buirski (1980) concluded that: '...selective pressures would operate to favour an organization of emotions in individuals which would facilitate social group living... the great similarity in organization of emotions in baboons, chimps and humans is evidence of the adaptive significance of this pattern.' He suggests that the pattern of emotions which fosters formation of a dominance hierarchy may be adaptive in the therapeutic group, by maintaining cohesion and stability, but the tendency toward rigidity of roles within the hierarchy may also inhibit personal growth, by precluding actualisation of the leadership potential of each member.

The mechanisms used in the formation of a dominance hierarchy could be maladaptive if aggression is not controlled. One mechanism which serves this function is the repertoire of submissive behaviours, indicating when one participant has lost; in most cases, with the emergence of these appeasement gestures, the aggressive behaviour of the superior individual stops abruptly. Similar phenomena have been observed in studies of elementary school children. "Behaviours found to precede the reduced probability of continued aggression typically involved a diminution of body stature in combination with lack of direct eye contact. Thus, to the extent that children's displays of aggressive behaviour in a playground situation represent at least one mode of human agonistic interaction, these results suggest that a number of human behaviours do exist which serve an appeasement function" (Ginsberg, 1980).

A second mechanism to control the extent of intra-group conflict is found in leader role behaviour: the dominant member is often observed to intervene as a referee when conflicts become so intense as to threaten group cohesion (Eibl-Eibesfeldt, 1975). In Ginsberg's study, it was noted that when an aggressor failed to heed appeasement signals from the child under attack, intervention by a third child was likely to occur. One might speculate that the intervening child is conforming to innate 'rules', related to the establishment of a dominance hierarchy; i.e. once appeasement has been signalled, further aggression is not only unnecessary but actually contraindicated.

Lieberman *et al* (1973), in their extensive study of encounter groups, found that the control or 'executive' function of the group leader is curvilinearly related to positive change in members. If the leader exerted too much control, the group became highly structured and authoritarian, failing to develop a freely flowing interactional style or member autonomy. Too little executive function, a *laissez-faire* style, resulted in a disorganised and structureless group. In addition, highly intrusive and confronting 'charismatic' leaders produced an elevated number of group casualites; by pressing too hard for emotional interaction, such leaders did not perform a satisfactory governing function in regard to the rate of affective stimulation. While the non-human and human studies are not directly comparable, the results of this encounter group investigation are compatible with the general hypothesis that the effective leader performs an important function in controlling interactional patterns, particularly conflict issues.

Group Stages and Hierarchies

Several authors (Beck, 1974; Tuckman, 1965; MacKenzie & Livesley, 1983) have identified stages of group development which appear to be common to a variety of human groups. The 'stage' hypothesis generated from this work provides a description of mechanisms by which a cluster of diverse personalities can be transformed into a social system. Natural selection would be expected to favour mechanisms in individuals which guide a group of individuals through a process resulting in a cohesive, well integrated survival unit.

Stage 1 in this model is that of group formation—the engagement stage. The task to be accomplished consists of transforming a number of individuals into a group which actively works together on a task that is perceived by individual members to have value, whether this be natural survival or psychotherapeutic exploration. For this to occur, the individual must be considered acceptable by the collectivity and must in turn view the group as having some advantages. This stage is characterised by the self-disclosure of selected aspects of participants' personalities and experiences, leading to a growing recognition of similarity among the members, which appears to mediate the development of cohesion. A generally positive emotional tone is observed, and conflict is notably absent until the engagement process is well established.

There appear to be a number of similarities between typical Stage 1 behaviours in non-human and human primate social groupings respectively. An innate tendency to avoid conflict on initial meeting can be observed in the greeting rituals of various primates: Van Hoof (1967) describes 'lip-smacking' and 'silent grin' facial displays, which may be interpreted as greeting rituals inhibiting conflict. He discusses the social function of this facial behaviour as follows: "In most species, the movement is not frequently seen between animals which are associated in an established relationship with one another.... It may be shown, however, quite frequently during a short time when the animals meet for the first time, or after a period of separation.... An approach is followed by mutual grooming, huddling together, play, mating or simply being in each other's neighbourhood.... As a rule the posture facilitates non-hostile approach between the individuals and this may be achieved by an appeasing or reassuring effect on the partner.... The display may reflect a conflict between the tendency to flee and the tendency to approach."

In the study by McGrew (1972), it was noted that newly formed groups of nursery school children exhibited a period of relative calm before the onset of aggression, and returned to a more quiescent state after dominance decisions had been reached. On the initial meeting, McGrew's subjects demonstrated shyness and 'nervous caution', accompanied by a spectrum of behaviours such as lowered head and avoidance of eye contact, which are characteristic of primate appeasement patterns. Studies of adult groups report rising levels of interpersonal warmth and comradeship, coupled with low levels of conflict during initial sessions (MacKenzie, 1983). The cohesive character of Stage 1 groups may express in innate phenomenon, closely associated with the more brief greeting rituals widely observed among the primates. It may be hypothesised that if a social system is to become established, these rituals have an important function in facilitating social bonding, before the potentially disintegrating effects of conflict occur.

Thus, if individuals who are not in an established relationship with each other come together and basic interactional safety is perceived, then appeasement behaviour in children and greeting rituals in adults are likely to occur. Such conditions may be met because of previous meetings, the presence of parental reassurance, or readiness to participate in a joint task such as psychotherapy. These appeasement behaviours and greeting rituals may have an important function in dampening or delaying the emergence of dominance conflict. From our consideration of therapy groups, this initial introductory stage is characterised by content themes emphasising similarity and universality; e.g. "I didn't think anyone else could have such thoughts; it's a great relief to know I'm not the only one". This cognitive dimension seems to be a correlate of appeasement behaviour.

The criteria by which the members of a newly formed group establish a sense of commonality are of a general and global nature; e.g. common geographical origins or interpersonal stressors are interpreted as evidence of high personal similarity. This process is important because it provides a means by which the members may safely identify with each other. The mechanism of allowing these assumptions to go unchallenged appears to achieve the same function as the facial and postural ritual greeting behaviour in non-human primates. Such displays indicate an adherence to rules of behaviour, and so indicate basic interactional safety. Since the human animal has the capability of more complex functioning of the central nervous system, the mechanisms to control conflict are manifested in verbal as well as facial and postural patterns.

There is strong evidence for the emergence of a stage characterised by competition, conflict, and anger after an introductory stage of engagement and orientation. This conflict or differentiation stage is also concerned with the clarification of group normative regulations and with agreement about how the group should operate. These phenomena appear to be descriptively similar to those occurring in the hierarchy stabilisation described by Eibl-Eidesfeldt (1975) in other animal groups. They may be hypothesised to have a similar objective of developing greater system stability by establishing predictable interactional patterns and social rules. This has been termed the 'differentiation stage' of group development (MacKenzie & Livesley, 1983), and the task is to acknowledge the place of the individual in the group system. The recognition of differences amongst members generates a climate of conflict and turmoil, which is generally accompanied by considerable anxiety; to progress through this stage, the group must develop an effective mode of conflict resolution. A prolonged competitive and unyielding approach will result in group fragmentation.

Stage 1 has functioned to bring the group members together, providing cohesion to weather the necessary tempests of Stage 2. It is now necessary to consider how the potentially disintegrating process of differentiation can be adaptive. To function in a natural setting, a group needs to delineate the capabilities of its members under conditions of duress; there must be a pattern for efficient decision making, a means of tempering conflict and intra-group aggression. The formation of a dominance hierarchy provides the group with these important survival mechanisms.

Resolution of dominance issues has as its cognitive analogue a focus on differences, revealed in such typical statements as "I don't see how you can say that; it really makes me angry; I would never dream of doing such a thing", or "I think it's high time we decided how the group should run and not just follow along like a bunch of sheep". The consistent emergence of these themes and the degree of affective arousal they produce suggest the operation of innate social mechanisms. There is also evidence to suggest that the therapist has a role of conflict mediation in this process, just as the high-ranking male in a baboon or rhesus troop has. The 'higher order' resolution which appears to operate in human groups involves an agreement to accept and discuss differences, and even to learn from them, rather than stamp them out. This has strong parallels with the acceptance of a dominance hierarchy which allows conflict to subside and more productive group cooperation to take place.

The concept of group developmental stages offers an alternative approach to understanding group-as-a-whole phenomena. The traditional approach has viewed group themes as centering around dynamic issues of relevance to the majority of group members. Such terms as "basic-assumption-group phenomena" (Bion), "common group tension" (Ezriel), and "group focal conflict" (Whitaker & Lieberman) have been employed (Scheidlinger, 1980). All of these theories make the somewhat dubious assumption that group interactional sequences can best be understood as manifestations of a single thematic issue which is common to all members, albeit with varying degrees of saliency. Developmental stages are viewed in terms of group tasks which members must deal with in their own fashion, if they are to be in step with other members of the collectivity. Since studies comparing these two approaches are not as yet available, group-as-a-whole and developmental theories are best considered as complementary ways of viewing the complexity of group events. Investigation of the relationship between group-as-a-whole phenomena and dominance hierarchies would be of particular interest.

The examples above from both non-human and human sources offer the opportunity for speculation about the precursors of behaviour observed in therapy groups. Such an evolutionary perspective may be of value in suggesting novel interpretations of common clinical phenomena. More complex phylogenetic forms frequently demonstrate behaviours based on patterns found in simpler organisms; for example, affective states are mediated through limbic structures in all mammals, but are subject to more complex associational and inhibitory cortical influences in higher primates.

There thus appears to be a number of social system phenomena which are found in both human and non-human primate groups, and the presence of such similarities suggests the operation of innate mechanisms held in common. These include: greeting rituals comprised of mutual appeasement behaviours; formation of a dominance heirarchy; and expectations concerning role behaviours of dominant members. However, in Stage 1 the submissive behaviours are used by both members of a dyad, whereas in Stage 2 they are seen primarily in the sub-dominant member. The behaviours characteristic of Stage 2 appear to be particularly overt demonstrations of the consolidation of a dominance hierarchy. For a social group to develop, two opposing adaptive processes must be reconciled—mechanisms for developing cohesion, and mechanisms for facilitating the confrontational rank ordering process. If social group behaviour is conceptualised from the standpoint of development phenomena, then Stage 1 is primarily concerned with cohesion issues and Stage 2 with dominance struggles, but appeasement behaviours appear to have an important function in the accomplishment of both tasks. The use of these mechanisms allows the developing group to coalesce without immediate conflict, and at the second stage allows dominance confrontation to occur without the disintegration of the system. Thus, the disintegrative aspect of hierarchy formation is balanced by the mechanisms of appeasement behaviour and by the moderating role of the leader. These patterns reflect a developing social structure, which provides the group with greater organisational stability.

Application to Therapy Groups

Regression induced by membership change

Eibl-Eibsefeldt (1975) observes: "Rank order... prevents continuous conflict between members of the group. Not until there is a disruption in this order can one observe outbreaks of intense aggression within a previously harmonious group". Bernstein *et al* (1974) introduced new members into a caged group of rhesus monkeys, causing a four-fold increase in aggression within the group, but this aggression could be diminished by introducing new members gradually. In humans, Barkow (1980) has hypothesised that under conditions of stress, especially when verbal communication is reduced, a group will return to the primitive kinds of conflict used during childhood to reiterate the hierarchy.

The group therapist should be alert to the emergence of conflict and competition at times of group disruption, such as loss or gain of members, and change of leadership. Predictably, the group will then return to 'pre-work' stages of engagement and differentiation, and both the leader and 'old-group' members may experience the regression from therapeutic work as a frustrating loss. Such an attitude may interfere with the necessary integration of new members and may lead to the group disintegrating. If new members are to become incorporated into the group, they must have the opportunity of experiencing engagement and differentiation phenomena with the entire group. 'Old-group' members have an opportunity for altruistic behaviour, which may in itself constitute a therapeutic event for them, and there is also an opportunity to clarify and rework tasks of the early stage. The group must regress if it is to re-emerge as a newly structured collectivity, with power to induce change in all its members. The therapist is responsible for monitoring and shaping this process and for re-establishing the stability associated with resolution of dominance hierarchy issues.

Loss of rank

Price (1967) hypothesised that depression is associated with a loss of rank in the hierarchy, and it may have an adaptive function in inhibiting further conflict. Since the loss of self-esteem and feelings of inferiority associated with depression effectively eliminate any desire to confront a superior, depression also serves as a shut-off device, preventing resurgence of dominance contests.

The depressed individual may be prevented from falling precipitously within the hierarchy by at least two mechanisms. The first is the characteristic irritability of depressed persons, usually toward inferiors; Price (1967) postulated that this helps the depressed to identify those who are still inferior in rank, thus buffering the fall. Secondly, the facial expression, posture, and voice tone of the depressed individual tends to induce a care giving response in group members—a "re-integrative" mechanism (Plutchik, 1980). Dominance issues will inevitably arise, and their resolution involves loss of rank for some members, but an established hierarchy provides stability within a group, and is associated with a decline in conflict. At the same time, the bruised self-esteem experienced by those relegated to lower rank may interfere with therapeutic objectives. Successful mastery of the second stage of differentiation is accompanied by a tolerance of differences and by open discussion of conflictual issues, promoting their resolution. Through this mechanism, the viewpoint of each individual can be acknowledged, thus balancing the potentially damaging effects of unavoidable dominance contests. This essentially cognitive process provides another example of the importance of more recently evolved cortical structures in modulating the effects of 'lower' emotional patterns. The therapist has an important function in ensuring that all group members have sufficient opportunity to present their unique position, and in ensuring that a response is forthcoming from other members.

Scapegoating

Van Lawick-Goodall (1971) has documented the tendency of chimpanzee groups to expel members who are deviant from the norm: a chimp with polio was ostracised by the group and finally abandoned. As the hierarchy is established, weak or abnormal individuals are relegated to the lowest position on the social ladder, suffering the greatest number of contest losses of any group member. In non-human primate groups, the phenomenon of 'redirected threat' occurs—a loser of a dominance contest becomes irritable and acts aggressively towards an individual of lower rank, the lowest ranking one receiving the greatest number of redirected threats.

Schmidt (1960) documented the cruelty of school children towards peers who are overweight or otherwise out of the norm.

In therapy groups, the role of the scapegoat serves as an absorptive sink for the projection of avoided, negatively valued, and frequently aggressive issues; the creation of a scapegoat may also serve to unify the group, as they gang up against the offending member. Occupying the lowest position in the hierarchy predisposes the scapegoat to severely dysphoric states of depression and anxiety. From the perspective of the development of a hierarchy, the emergence of a scapegoated figure represents an extreme polarisation along the dominance axis, and such a pronounced scapegoating process indicates a group in an avoidant and defensive position, requiring the active intervention of the therapist. The deviant member needs an understanding and supportive approach, even if he is unable to acknowledge such positive overtures. At the same time, the therapist should seek to stimulate an exploration of differences amongst the other group members.

Inhibitive influence of the dominant member

In baboon groups, Kummer (1971) has observed evidence for social inhibition which reduces an animal's tendency to perform a behaviour when it sees another group member already attending to it. "When a group has a leader, another male may not lead the group or scan the surroundings until the day that leader dies, but when this happens, he may take over the leader's role within hours. One must assume the previous leader's activities inhibited leading behaviour in the other members of the group". Not only certain role behaviours, but perhaps also cognitive abilities might be inhibited among lower ranking individuals, in the presence of a superior; for instance, primates are seldom observed to challenge the decision of the dominant males as to which direction the group should travel. These observations would suggest that the therapist might strive to rotate the role of leader among all group members, to decrease the inhibiting influence of superiors.

Conclusion

Analysis of the pioneering field studies of non-human primate social behaviour carried out over the past 25 years, from the perspective of group function, allows new hypotheses to be generated for the investigation of human behaviour. Group cohesion and interpersonal conflict may be considered fundamental polarities of social interaction, and these two opposing tendencies are dynamically balanced in the development of a dominance hierarchy. This process of rank ordering is a pervasive social phenomenon, widely studied in non-human primate groups but so far largely overlooked in human clinical studies.

The application of these concepts to clinical work must therefore be speculative, but this material may still be of value in conceptualising a number of common clinical phenomena such as: the accomplishment of group developmental tasks; regression induced by membership change; the effects of loss of social rank; the process of scapegoating; and the inhibitive influence of the dominant member.

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James L. Kennedy, BSc, MD, *Resident in Psychiatry, Department of Psychiatry, Yale University, USA.*

*K. Roy MacKenzie, MD, FRCP(C), *Professor of Psychiatry, Faculty of Medicine, University of Calgary, Calgary, Alberta, Canada T2N 1N4.*

*Correspondence

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Psychiatry in the People's Republic of China

WILLIAM LL. PARRY-JONES

In the spring of 1985, a party of psychiatrists from Great Britain and Ireland visited four major Chinese cities—Beijing (Peking), Shanghai, Nanjing (Nanking) and Guangzhou (Canton), as a study tour of the Royal College of Psychiatrists, under the auspices of the Chinese Medical Association. A number of psychiatric hospitals were visited and there was opportunity for many discussions with psychiatrists and other professional staff. This paper records some impressions of the psychiatric services and practices that were observed, together with material obtained in discussions. It is hoped that it will update and complement previous reports by Western visitors to China, and thus increase understanding of mental health in China.

The People's Republic of China was founded in 1949, after the Communist victory ('Liberation'); a period of massive land reform and economic development followed and, in 1958, both industrial and rural sectors were reorganised into communes. The Cultural Revolution began in 1966 and profoundly affected the health care system, particularly as a consequence of the efforts to de-professionalise and decentralise services; it was at this stage that peasant health workers, known as 'barefoot doctors', were introduced. A decade of turmoil and experimentation ended with the death of Chairman Mao Zedong in 1976, and has been followed by a major programme of 'four modernisations'—to upgrade national performance in industry, agriculture, science and technology, and defence. The impact of these policies has been remarkable, with increasing prosperity accompanying the rapid technological progress; within medicine, greater emphasis has been placed on research and on the quality of professional training.

The current provision of health services needs to be viewed in the setting of some unique features (Crammer, 1985). China is a vast country, with relatively poor transport and communication systems. The huge population of 1,000 million is distributed unevenly, being concentrated in the eastern parts of the country, and despite the enormous size of many cities, is predominantly rural.

The current provision and administration of health services is multi-tiered, and is linked closely with the system of government, from central to local levels (Chen, 1984). In rural areas, the Commune system has been of central importance for many years, although this is now much diminishing. Up to 40 families make up a Production Team, and seven or eight Teams constitute a Production Brigade, which is responsible for organising co-operative medical stations or clinics, staffed chiefly by paramedical workers, who are now referred to as 'country' doctors and have three to six months' training. The clinics form the basic tier of rural medical and health delivery organisation. The Commune itself comprises up to 15 Brigades, and is responsible largely for the provision of small rural hospitals; larger general hospitals, of up to 400 beds, are provided by the Counties.

In the cities, there is a similar three-tier service: primary health care is provided in health stations, at the place of work or run by neighbourhood committees. The next tiers are made up of district and county hospitals and, finally, municipal hospitals, which include special institutions such as psychiatric hospitals. Medical services appear to be free, although travelling expenses and subsistence costs have to be borne by patients; however, these costs may be subsidised from commune or production brigade welfare funds and from contributory schemes.

Psychiatric Services

The asylum system was introduced into China at the end of the nineteenth century by medical missionaries, and began to replace traditional methods of care in some areas (Young & Chang, 1983; Koran, 1972). The first mental hospital in China was the John Kerr Hospital, founded in 1898 by Presbyterian missionaries at Guangzhou, and subsequently another was opened in Beijing in 1906, where a Department of Psychiatry and Neurology was set up in the Peking Union Medical College in 1930. Several accounts suggest that by 1949, there were mental hospitals in only four cities (including Nanjing and Shanghai), providing about 1000 beds, though Xia & Zhang (1981), state that this is an under-estimate. Subsequently, psychiatric services began to expand progressively throughout the country and by 1959, there were 62 psychiatric hospitals. In 1958, an important National Conference for the Prevention and Treatment of Mental Diseases was held at Nanjing and this gave added momentum to psychiatric developments.

The Cultural Revolution led to major changes in both theory and practice, with undoubted diminution in the quality of care (Young & Chang, 1983), but after 1976, with the downfall of the Gang of Four, progress was resumed rapidly, hastened in 1978 by a National Symposium on Neurology and Psychiatry in Nanjing. In the early 1980s, new mental health institutes were established in Beijing and Shanghai and, in addition, there was rapid development of professional training as well as greater contact and exchange with Western psychiatrists. At present, psychiatric services are provided principally by psychiatric hospitals in municipalities, districts, provinces, and counties, and by the Departments of Psychiatry in teaching hospitals, associated with medical colleges.

The main emphasis has been on the development of adult services, with very slow extension of child psychiatric provision, and there are still no separate services for adolescents. The accounts of services in Sichuan by Liu (1980) and by Crammer (1985) provide a useful introduction to the provisions in one province. In the cities visited by the College group, the psychiatric hospitals comprised acute treatment wards and outpatient departments on central sites, with longstay hospitals in the suburbs. In addition, there are large sanatoria, catering for chronic diseases, where psychiatric patients may be admitted. Community and preventive work was said to have been receiving increasing attention in the large cities, undertaken in primary mental health stations, run by municipal mental hospitals and by medical college departments of psychiatry. (The College group did not have the opportunity to visit a mental health station or a sanatorium).

The staffing of the psychiatric services comprises psychiatrists, nurses, and a very small number of clinical psychologists; there are also few psychiatric social workers and, in the hospitals visited, occupational therapy appeared to be undertaken by nursing staff and untrained workers. Full Western-type medical training takes at least five years, the longest being of eight years' duration, at the Capital Hospital, Beijing; it generally includes two weeks' psychiatric experience, in addition to 27 hours of lectures. Postgraduate trainees are assigned to specialities. Provinces are responsible for postgraduate training, in which up to three years can be spent as a resident doctor, including a year of apprenticeship training. Thereafter, the psychiatrist is likely to become a visiting doctor at other hospitals: this is a specialist post, which can be held for a long period, until promotion to more senior appointments. There are no specialist accrediting bodies.

Recent reports of psychiatric manpower (e.g. Young & Chang, 1983) indicate that there are 400 senior psychiatrists and 3000 other doctors, many of whom have not received full medical college training, treating 60,000 inpatients. The basic training of nurses takes three years; those choosing or directed to enter psychiatric nursing receive further training on an in-service basis, lasting three to four years; there appears to be no centralised nursing examination system. Several hospital nurses expressed interest in learning more about the management of non-psychotic disorders and, whilst some nurses work in the community, they appeared to be concerned largely with following-up and giving medication to chronic psychotic patients. It was difficult to gain a full impression of the work of clinical psychologists in psychiatric hospitals, although psychological testing appeared to be favoured; according to Brown (1980), Chinese psychology has a strong behavioural and experimental orientation. Crammer (1985) reported that there were no clinical psychologists in Sichuan, although educational psychology was well established.

Considerable interest in research was expressed in all the centres visited, the principal subjects under consideration being the genetics, biochemistry, and electrophysiology of psychiatric disorder, as well as psychopharmacology. There has also been major emphasis on both epidemiological work and clinical investigations; a useful summary of recent research is provided by Liu (1984). However, research departments appear to be very small, and the research being undertaken is limited because of the lack of funding, equipment, and trained personnel. The principal vehicle for scientific publications is the Chinese Journal of Neurology and Psychiatry, founded in 1955. In keeping with most scientific journals, it ceased publication during the Cultural Revolution, but resumed in 1978.

Theoretical Background

In traditional Chinese medicine, the main influences in the causation, diagnosis, and treatment of illness have been concerned with Taoism, Buddhism, Yin and Yang, and the five elements (the seasons and weather, spirits and demons, emotions, trauma, hunger, and overeating) (Koran, 1972). Of particular importance were the opposite elemental forces—Yin and Yang—which were thought to flow in a network of channels connecting internal organs with points on the skin, knowledge of which still underlies the practice of acupuncture; if they were balanced and in harmony, health was maintained. In addition to medicines, traditional treatments included acupuncture, moxibustion (*vide infra*), exercises, and massage, all of which were through to influence the flow of the Yin and Yang. The inter-relationship of these concepts at the present day is especially complex, particularly when it comes to the generation of mental illness; the place of psychiatry in traditional Chinese medicine has been well reviewed by Veith (1955), Tseng (1973), and Liu (1981).

Western influence, beginning at the turn of the present century, brought with it diverse views, including Freudian and Meyerian, although the impact of psychodynamic theories was to be minimal. Following the 1949 Revolution, Marxist–Leninist ideology and the teachings of Mao Zedong were prominent. In the 1950s, Russian intellectual influence was substantial: Pavlovian theory, ideological indoctrination, and work therapy were widely employed, and Western-style psychology fell into disfavour. Following the Sino-Soviet rift in the early 1960s, the Pavlovian influence diminished, though during the Cultural Revolution, some forms of psychiatric disorder came to be construed as manifestations of faulty political thinking, to be treated by political re-education. Attitudes towards Western medicine were negative and for many years, academic exchanges were minimal; however, Taipale & Taipale (1973) have described in detail a visit to Shanghai at this time during which their hosts were willing to discuss all aspects of their work except, for apparently political reasons, their aetiological views.

Since the end of the Cultural Revolution, emphasis on socio-political forces in mental health has much diminished. Although it remains difficult to obtain a clear view of the accepted meaning of mental illness (Brown, 1980), the principal emphasis is now on biological determinants of disorder and on causative theories which presume genetic and constitutional factors, rather than intrapsychic, interactional, or situational ones. The national approach to psychiatry is thus almost Kraepelinian in its style, giving great attention to accurate observation and description. Many of the psychiatrists who were encountered during the College visit postulated some form of brain dysfunction as the central disorder which, in turn, was responsible for a variety of psychological and physical symptoms. Neurosis, therefore, could be regarded as a chronic functional disturbance of higher nervous centres. Cautious views were expressed about the possible adverse effects of environmental influences, while psychodynamic theories were given little attention; in fact, psychoanalysis has been much criticised for its non-scientific basis, and has been widely rejected, broadly in keeping with Marxist critiques of psychoanalysis in the West, so that the concept of unconscious motivation is hardly employed in China.

In 1963, the textbook *Clinical Psychiatry* by Mayer-Gross, Slater & Roth was translated into Chinese, and has been subsequently very influential; more recently, works by Fish and Lishman have been popular, and in child psychiatry, the textbook edited by Rutter & Hersov is in use. It was reported to the delegation that a substantial series of textbooks on contemporary Chinese psychiatry is in preparation. As far as could be ascertained, classification of disorders is broadly similar to that in the International Classification of Diseases (ICD-9) (Chinese Medical Association, 1982), but there is also familiarity with the categories of DSM-III.

Psychiatric Centres Visited

Beijing Anding Psychiatric Hospital (opened as a private hospital in 1917), a municipal hospital, has a total of 1600 beds and 1600 staff. It comprises three parts—an urban hospital and outpatient department, a 30-bed child psychiatric ward, and a large suburban branch, with acute and long-stay beds; the latter two were visited. It is the teaching hospital of Beijing Union Medical College, funded initially by the Rockeffeller Foundation, and in addition, offers postgraduate training and research facilities.

Nanjing The Neuropsychiatric Hospital (founded in 1947) is a large complex with 580 beds, close to general hospitals, comprising departments of neurology and neurosurgery, general psychiatry (1100 admissions annually), social psychiatry, forensic psychiatry, and child psychiatry. The latter is housed in the Nanjing Child Mental Health Research Centre (opened in 1984), which is the principal child psychiatric centre in China.

Shanghai The Shanghai Psychiatric Hospital (opened 1958) and Institute of Mental Health (opened 1982), form part of a large municipal hospital complex, treating 4000 inpatients annually and 500 cases daily in the outpatient department. It has 880 beds and 1400 staff, including 119 psychiatrists, 515 nurses, and 70 technicians. Only five child psychiatrists work in Shanghai, with a few interested paediatricians; there is a ten-bedded ward for children, but this was closed for repair at the time of the College visit. This is a teaching hospital for the three Shanghai Medical Colleges, but the Institute of Mental Health is primarily a research centre. This hospital has been visited by numerous Western visitors and Brown (1980) has summarised the main findings of 15 different visits, as well as findings in Tianjin and Beijing (see also Ratnavale, 1973; Sainsbury, 1974). There is extensive involvement in community work in the city, with approximately 15,000 chronic patients being cared for. A coordinating committee for mental health links municipal, district, and neighbourhood resources and provides advice on therapeutic and preventive measures for patients in the whole municipality. This hospital is linked with a branch hospital for long-stay patients and with three sanatoria.

In addition, there are 22 district and county psychiatric hospitals in Shanghai, each with 60–100 beds, none of which were visited; altogether, there are 5,300 psychiatric beds for the total population of 12 million. According to Xia (1983, unpublished), the community mental health care services in Shanghai comprise "occupational therapy groups and welfare workshops", which are day centres, providing psychiatric treatment, rehabilitation, and crisis intervention; as well as a network of "psychiatric home care units", providing home visiting and treatment, and "mental patients' care groups" for employees in large factories. These services rely on volunteers and paramedical personnel, who are given short courses of psychiatric training. The delegation did not have the opportunity to visit any of these services, but Thornicroft (1986) has provided an up-to-date impression.

Jiading Outside Shanghai, in one of the neighbouring counties, the Jiading County Mental Health Hospital was visited. This was opened in 1974; it has 100 acute and 30 long-stay beds to provide for a total population of approximately 500,000 (19 Communes), and is staffed by 13 doctors.

Guangzhou No hospitals were visited in this city, but, as in the other centres, a lengthy meeting took place with psychiatric staff. The hospital in the city dates originally from the late nineteenth century. At present, it has 1500 beds (700 chronic, 800 acute), a busy outpatient department with 600 patients daily, and a total staff of 1000, with 120 doctors.

Utilisation of Psychiatric Services

Substantial differences between China and the West in the pattern of recognition of mental illness make it very difficult to comment on prevalence. Chinese Ministry of Health figures for 1978 indicate a rate of treated mental illness of 5–7 per 10,000 (Sidel & Sidel, 1982). It is interesting to compare this figure with the very detailed statistics maintained at the Jiading County Mental Health Hospital, where the prevalence of psychiatric disorder in the community was recorded as 6.96 per 1000. It is quite clear, though, that the range of problems presenting for professional psychiatric treatment is significantly smaller than in Europe. This fact has to be seen in the context of the social, economic and political organisations, as well as the cultural traditions of contemporary China: the family, neighbourhood and workplace groups and committees play a significant part in the management of an individual's personal and interpersonal problems. In this way, community mental health programmes depend heavily on non-psychiatric resources. At Production Brigade level, both lay and paramedical workers undertake intervention and counselling, but problems outside their scope are seen at county hospitals or at district mental health stations in cities.

Patients are usually taken to hospital by their relatives, friends, or colleagues, or by their co-workers in factories and communes. The principal psychiatric hospitals are at provincial level, although some county and district hospitals have psychiatric beds. Only the more severely disturbed patients are admitted to hospital, and this is clearly part of an attempt to focus resources on those most likely to benefit. Most chronic patients are treated as outpatients; these departments appear to be exceptionally busy with, for example, 600 patients being seen daily at the Guangzhou Psychatric Hospital. There is no legal provision for compulsory admission and detention; however, patients are admitted and held against their wishes, though only with the agreement of the family, when they are suicidal or dangerous. Most of the wards in the hospitals visited were locked, and there were occasional examples of the use of simple physical restraint, e.g. whilst receiving acupuncture. The average length of stay in the acute treatment wards in all the hospitals visited was reported to be of the order of 3–4 months. Visiting by relatives, several times a week, was encouraged.

The majority of the inpatients in the hospitals visited were diagnosed as suffering from schizophrenia, e.g. in Nanjing the proportion was said to be 80%. Many other reports confirm the much higher proportion of schizophrenics in Chinese hospitals compared with Western inpatient samples, even when modern diagnostic criteria are applied

(Yan *et al*, 1984); this may be partly explained by the admission policy, whereby priority is given to severely ill patients. Low numbers of affective disorders (3–5%) were reported to the delegation, as recorded by many other observers, some of whom have suggested that Chinese psychiatrists underdiagnosed manic-depressive illness and overdiagnosed schizophrenia, though Yan *et al* (1984), using DSM-III criteria, reported 22.4% at the Zhen Jiang Psychiatric Hospital, Jiangsu Province. The characteristics of mania in Chinese patients were described by the same authors (1982).

Elderly and demented patients are cared for largely at home, in keeping with the principle that the young look after their older relatives, whilst those without relatives are provided for separately in the community. In Beijing, for example, under 5% of inpatients at Anding Hospital were over 60 years of age. There appears to be a stigma attached to placing old people in institutions other than for acute medical reasons, though it is recognised that the strain on the carers will increase with the trend towards women working outside the home. In country areas, where there is little danger to be encountered from wandering in a closely-knit community and where problems from inefficient use by old people of modern appliances rarely occur, there are few complaints of psychogeriatric difficulties. Chinese psychiatrists indicated that old age psychiatry was likely to be needed in the future, but the current priority had to be given to younger age-groups. There were no psychogeriatric wards in the hospitals visited, though some long-stay wards contained a number of aged patients, who were not significantly demented and appeared to be manic-depressives or longstanding schizophrenics.

It is claimed consistently that alcoholism and drug addiction are now very rare in China and that admissions to hospital for those reasons are very infrequent; at Anding Hospital, it was stated that in the last 20 years, only 35 alcoholics had been admitted. As recently as 1949, there were reported to be 49 million opium abusers in China (Cerny, 1965), and it does appear that this vast problem has been overcome (though perhaps partly by emigration). Patients with personality disorders are rarely admitted, since such problems are considered to be social and community matters. Neurotic disorders are not regarded as common, and are mainly treated on an outpatient basis; in the past, the most prominent neuroses were thought to be hysteria and neurasthenia. In Jiading, it was reported that over 12% of patients admitted were suffering from hysteria. In 1985, reference was still being made to the frequency of neurasthenia; since this is viewed as essentially a physical disorder, it is likely that a range of conditions that would be regarded as psychiatric in the West are being accepted as medical illnesses under this general heading and treated in general medical and neurological settings (see Allodi & Dukszta, 1978). Many studies have indicated the strong tendency for psychiatric disorders in China to present as physical complaints and that such somatic conceptualisation of disorder influences the choice of health care service utilised (Kleinman & Mechanic, 1979). Suicide statistics were not made available, but the rate was claimed to be low, with hanging or jumping off high buildings as the most common methods. The problem of parasuicide appears not to occur on anything like the scale that it does in Western countries. Anorexia nervosa is considered to be very rare: in Shanghai, for example, the visitors were told that only seven cases had been diagnosed in 27 years, and this low incidence was attributed to major socio-cultural differences between China and Western countries—in China, fatness is still a symbol of health and prosperity. When the disorder occurs, it is treated with chlorpromazine and psychotherapy combined. The management of epilepsy is often seen as part of psychiatric practice, most patients being treated as outpatients. It appears that sexual deviations are rarely encountered in the psychiatric services, and homosexuality is illegal.

These observations, made in 1985, about presenting disorders are comparable with previous reports. Young & Chang (1983), reported the following statistics for inpatients from Hunan: schizophrenia 50–70%, other functional psychoses 10–15%, organic disorders 10–15%, neuroses 5%, miscellaneous diagnoses 5%. With regard to outpatient populations, they suggested that 50% were neurotic, and 80% of these were classified as suffering from neurasthenia.

The practice of forensic psychiatry is very limited in China, although psychiatric assessment of criminal offenders is being undertaken, and Crammer (1985) noted the increasing importance of forensic psychiatry in Chengdu. According to Liu (1984), "The Chinese Criminal Law, issued in July 1979, provides that the psychotic patient, who cannot identify or control his own behaviour, has no responsibility for hazardous consequences caused by his behaviour, but the psychotic patient in intermittent period remission is responsible for his criminal acts". These statements are incorporated in *The Criminal Law and Criminal Proceedings Law of China* (1984). No Special Hospitals for the treatment of criminal patients were reported in the cities visited.

General Observations about Hospitals Visited

The psychiatric hospitals in Beijing, Nanjing, and Shanghai took the form of large, functional blocks, mostly built within the last 40 years. In the adult wards, male and female units were segregated, although there were said to be opportunities for social contact. In the acute treatment areas, the units usually comprised 60–70 patients and, generally, were made up of a day room, which doubled as dining and occupational activity area, and attached dormitories. The wards were clean and not overcrowded, although by Western standards, they were relatively bleak, with unupholstered furniture All day rooms had a TV set, concrete floors, barred, curtainless windows, bare, whitewashed walls, and limited or no heating (in spite of very cold winter temperatures).

The dormitories were either open, or broken up by simple partitioning; some had lockers, but no personal possessions were displayed, and the beds were made up in a scrupulously uniform fashion. Conditions were noticeably more basic in the Jiading County Hospital than in the cities. Each ward had one or two single rooms for the management of difficult patients, though few violent ones were said to be admitted. All patients were uniformly dressed in hospital clothing, taking the form of baggy, pyjama-like suits; similarly, doctors and nurses were usually dressed in white overalls and skull caps, without distinguishing insignia. Though generally closely supervised by nurses, the patients appeared tranquil, friendly, and obviously delighted to greet visitors and keen to practice their English. In the ward areas, patients were largely engaged in group-based activities, talking and working.

The hospital day appeared to be well structured, with emphasis on work therapy, exercise, and recreation with games like chess and table-tennis. Small groups of patients were engaged in outdoor gardening and maintenance projects. There was evidence of considerable attention to detail in keeping patients' records and treatment schedules and in displaying statistical information; the latter was especially notable at the Jiading County Hospital. Laboratory and other diagnostic and support services seemed limited at all the centres visited, although there was evidence of new equipment being introduced gradually. There was a large, actively-used psychiatric library at the Shanghai Psychiatric Hospital, though it seemed to be largely dependent on gifts of overseas publications.

Treatment Methods

At the Nanjing Conference in 1958, it was decided to "discard locking up and tying up the psychiatric patients and use four kinds of treatments instead" (Liu, 1984). These comprised a combination of traditional and Western medicine and physiotherapy, work therapy, physical exercise and recreational therapy, and planned educational therapy. Although the socio-political situation has changed considerably since then, the essential components of treatment remain much the same.

Chinese traditional medicine

Traditional methods were advocated strongly during the period of the Cultural Revolution; their use continues in psychiatry, but appears to be regarded largely as an adjunct to Western methods and their efficacy seems to be viewed with some caution. In the country branch of Anding Hospital, Beijing, there are special wards for the combined use of traditional and Western methods, and this is probably widespread practice.

Medicinal herbal remedies have formed the mainstay of Chinese medicine for centuries, but there do not appear to be many drugs specific for psychiatric disorders. Instead, it seems that their main function is improving the patient's general health and resistance to disease. All hospitals have herbal sections in their pharmacies. Liu (1984) referred to several drugs in active use, including extract of *wikstromia chamedaphne meissn* in insomnia and neuroses; extract of *datura metel* and *datura innoxia* for violence in psychotic patients and a traditional prescription for "activating stagnant blood" in periodic psychosis. Of particular interest is the use in Sichuan of *parasiticus on coriaria sinica maxin,* which induces seizures and vomiting, in schizophrenia (Liu, 1980). In Beijing, it was reported that herbal preparations are used in the treatment of tardive dyskinesia, but it was not easy to establish the types of preparations used or their alleged function.

Acupuncture appears to be in widespread use in psychiatric treatment, although no clear scientific hypothesis has been advanced to explain its diverse applications. Intensive experimentation with acupuncture was undertaken during the period of the Cultural Revolution, when there was insistence on the use of traditional techniques. During the visit, individual patients and groups were observed receiving electro-acupuncture, in which a small current is passed through the needles from a regulator box for 15–20 minutes. The principal therapeutic objectives were the treatment of schizophrenia, states of excitement, hysteria, and insomnia. In schizophrenia, the most frequent sites for needles were the wrists and calves. In Beijing, patients were observed with needles placed just anterior to the external auditory meatus for the treatment of auditory hallucinations, and around the mouth in a chronic schizophrenic patient who was refusing food. Moxibustion—the application of heat to the skin by burning sticks of powdered mugwort wormwood (*artemesia vulgaris*)—and cupping were observed in a Commune Hospital in Jiading near Shanghai, in the treatment of muscle pain and stiffness, but they are not employed in psychiatric treatment. Other Western observers (e.g. Brown, 1980) have noted the use of various traditional methods in psychiatric treatment, such as yoga, breathing exercises, shadow boxing, and relaxation.

Western treatment methods

Acutely ill patients are treated vigorously, with the expectation of relatively short stay. Psychotropic drugs, including antidepressants, minor tranquillisers and neuroleptics are used widely; they are manufactured in China and only supplied from hospital pharmacies. Medication, especially with chlorpromazine, trifluoperazine, haloperidol and sulpiride, forms the mainstay of the treatment of the psychoses; depot preparations are in general use. Lithium is used in affective states, but monitoring of serum levels is complicated by the relative lack of laboratory facilities (Yan, 1981). Electro-convulsive therapy appears to be employed to a diminishing extent in the treatment of depression; when used, it is commonly in an unmodified form. Insulin coma treatment for schizophrenia continues to be employed, but probably on a very small scale. Psycho-surgery is not practised. In Nanjing, it was interesting to observe the use of dehydration, induced by diuretics, in the treatment of excitement, as well as intravenous hydrocortisone in the treatment of hallucinations.

Despite the absence of psycho-analytical methods, forms of individual counselling and psychotherapy do constitute an important part of management. Individual 'heart to heart' talks with doctors are used to provide an understanding of illness, so that it can be controlled. These are also intended to give support and to encourage confidence in overcoming personal and interpersonal problems and in functioning effectiely in one's proper social role, which may involve submerging one's individual self and personal interest in work and service to others. Family unity and service to the state are important ideals; self-control is a central feature and cartharsis has no part to play (Dien, 1983). Some of the ideology of revolutionary optimism, so prominent during the Cultural Revolution, lingers on despite the changed political scene. These concepts also appear to be central in group discussions, which form an important component in ward-based activities. Wards in Shanghai featured prominent notices on how to resume normal life and work after discharge, with advice about outpatient attendance.

Western concepts of family therapy, especially those in which emphasis is placed on self-revelation and emotional expression, are not employed, although it is clear that direct advice and counselling is provided for relatives. Behavioural methods were reported to be used, e.g. in the treatment of obsessive neurosis, and a simple token economy system was being employed in the children's ward at Beijing. The concept of productive labour is important in Chinese society and, not surprisingly, is reflected in the use of occupational therapy in psychiatric hospitals. All the hospitals visited had active ward-based and central work therapy departments. The tasks ranged from simple activities such as unpicking fabric to craftwork, metal work, and book binding. In addition, in large cities, occupational therapy stations in the community are said to contribute to rehabilitation, though these were not visited.

Child Psychiatry

In recent decades, substantial efforts have been made to enhance maternal and child health; infant mortality is now lower than in other Third World countries. There has been major concern about restricting population growth, and the one child family policy promotes actively the importance of one well nurtured and well educated child. Increasing provision is being made for pre-school facilities in nursery schools and kindergartens up to the age of seven. Primary schooling extends from seven to 12 years, and middle schooling thereafter up to 18 years.

From infancy, emphasis is placed on discipline, self-control, conformity, and on curbing independent activity and extremes of self-expression. According to Dien (1983), "The self does not develop in a process of gradual separation and individuation, as is often conceptualised in Western psychological theories. We see, instead a 'little me' maintaining its inderdependency within the context of the 'big me'—i.e. the family, the state and the world, throughout the life-span". Special attention has not been given to adolescent maturation, as it has in the West, and the whole process of individuation is restrained and played down. In fact, there is no separate term for 'adolescence' in the Chinese language, and the cult of youth has never been a feature (Butterfield, 1982). This has a bearing on the fact that adolescent adjustment difficulties do not feature significantly in the work of the Chinese child psychiatrist and, although rapid socio-political changes are now taking place, obtrusive adolescent behaviour was not observed in the cities visited, though it was in a commune centre. Moreover, many of the personal and interpersonal problems that present to the Western psychiatrists are dealt with in China within the social and political system.

Since 1949, rudimentary child mental health services have been developed, although it is reported that child psychiatry was not favoured during the Cultural Revolution. As far as can be ascertained, there are departments of child psychiatry only in Beijing, Nanjing, Shanghai, Guangzhou, and Harbin. Precise figures are not available for the number of inpatient beds, but they probably do not exceed 150, and there are only about 20 specialist child psychiatrists in China. Even if these figures are a serious under-estimate, they do not reflect accurately the volume of work being undertaken with children and adolescents, since outside specialist centres, psychiatrists practise as generalists, seeing patients of all ages as a matter of necessity. In Jiading County Hospital, for example, where there is no child psychiatrist, patients over 14 years are admitted to adult wards, the younger ones being treated as outpatients.

In 1984, the Nanjing Child Mental Health Research Centre was opened; it is the principal training centre for child psychiatry in China, attracting trainees from the whole country, who spend six months here: the immediate aims is to have one or two child psychiatrists in each of the 21 provinces, five autonomous regions, and three municipalities. The Children's Ward of Anding Hospital, Beijing, opened in 1964, has 30 beds for children aged seven to 17, and a busy outpatient department. Patients are drawn from a huge catchment area, extending hundreds of miles from the city. There are 20 staff, comprising four doctors, 15 nurses, and a teacher, with a social worker in the outpatient department; there are about 130 admissions annually, and the mean-stay is two to three months. Disturbed boys over the age of 14 are rarely accepted, being admitted instead to adult wards, but older girls are accepted. In Nanjing, a child psychiatry outpatient clinic was opened in 1954 and an inpatient ward four years later. The Child Mental Health Research Centre now comprises an outpatient clinic, a parental counselling service, day care and boarding provisions for retarded children, and a 50-bedded inpatient ward, which receives patients from all parts of China. Although the modern building was somewhat bleak, there was much more colour than in adult wards, and the atmosphere was friendly and lively. The staff includes psychiatrists, nurses, special teachers, and a person described as a social worker, who is in charge of occupational therapy. The Centre has active teaching and research programmes; it is particularly interested in genetic factors and in the relationship between family size and background and child mental health. There is a collaborative project with the Department of Psychiatry, University of Hawaii. It was at this Centre that the clearest view was expressed about the importance of psycho-social factors in child mental health (Tao, unpublished).

The outstanding clinical disorders amongst outpatients are said to be hyperactivity, mental retardation, and epilepsy; in both Shanghai and Nanjing, 70–80% of children seen as outpatients were considered to be suffering from the hyperkinetic syndrome, with an age of onset of 5–8 years, and characterised by poor school record, restlessness, inattentiveness, and 'soft' neurological signs. In 1982, research in Nanjing indicated that 3% of schoolchildren were hyperkinetic, and the disorder is thought to have been increasing over the last five years; it seems to be regarded as multidetermined with possible genetic, traumatic, educational, family, and environmental factors. Medication with methylphenidate or pemoline is commonly employed. Anti-social conduct disorders are very rarely treated, since they are generally managed in normal schools or in juvenile reform schools. Although informants indicated that juvenile delinquency was not a major social problem, there are signs that this was an under-statement, e.g. official statements in the press following an episode of soccer hooliganism in Beijing in May 1985.

Child inpatients appeared to be suffering mainly from schizophrenia, affective psychoses, and epilepsy, with small numbers manifesting hysterical and other neurotic symptoms. Of the 1435 children admitted to the Nanjing Centre between 1958 and 1983, 31.5% were diagnosed as childhood schizophrenia and 14.6% as mental retardation with psychotic manifestations. Cases of infantile autism were rare. Anorexia nervosa appeared to be extremely rare, but the very small number of cases described had the classical features of the disorder. Gilles-de-la-Tourette syndrome was reported to be relatively common, as well as a specific type of periodic psychosis, taking the form of premenstrual mania-like states in teenage girls, with psychomotor excitement and hallucinations, lasting about a week (Liu, 1984). Psychiatrists in Shangai reported that an eight-year follow-up study of the latter disorder showed that 10% of the patients developed schizophrenia and the remainder recovered partially or completely.

Treatment methods in child psychiatry include psychotropic medication, acupuncture, and ECT, which was given without anaesthetic in Beijing. A simple token economy system was in use at Beijing, all inpatients being rated weekly for their application to study, discipline, unity, health, and labour, and rewarded appropriately. As in the adult departments, occupational therapy and recreation are emphasised. Relatives are encouraged to visit several times a week. In view of the large distances travelled by patients to Beijing, it is customary for parents to stay in the city for the duration of the admission.

Mental Handicap

The prevalence of mental handicap was reported to be 1.1. to 5.2 per thousand, in five major cities in the 1970s (Liu, 1984). There appear to be very limited special services for the mentally retarded, the majority being dealt with at home and in the community, where day and residential education may be available. Severely retarded children were said to attend special schools or institutes, though these were not seen. The Nanjing Child Mental Health Research Centre provides a small daycare clinic and a residential school for retarded children, but the grounds of selection for admission to these facilities were not clear.

Conclusions

Chinese psychiatry has been subjected to a number of very powerful influences this century, and it is fascinating for Western psychiatrists to observe and to learn about the blend of emerging theories and treatments. The shortage of well-trained psychiatrists and the limited range of psychiatric hospital facilities restrict the existing services, which are hard pressed to cope with the most severely disturbed patients. Nevertheless, technologically developed countries can learn from the method of delivering primary health care services and especially from the way in which many disorders continue to be managed within the family and the community. The relatively small number of people apparently hospitalised for psychiatric illness points to very different attitudes towards disorder and deviance in this society, though it is not known to what extent this represents a burden on the community. In recent years, there has been a rapid expansion of exchanges between Chinese and Western psychiatry: this is to be encouraged strongly, as it advances knowledge and understanding, particularly of the relationship of culture to psychiatry.

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William Ll. Parry-Jones, MA, MD, BChir, FRCPsych, *Consultant Psychiatrist, Highfield Family and Adolescent Unit, Warneford Hospital, Oxford OX3 7JX, and Clinical Lecturer in Psychiatry, University of Oxford.*

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Levels of Expressed Emotion and Relapse in Depressed Patients

JILL M. HOOLEY, JOHN ORLEY and JOHN D. TEASDALE

The relationship between spouses' levels of expressed emotion (EE) and relapse was examined in a sample of 39 depressed psychiatric hospital patients. Over a nine-month follow-up, 59% of patients with high-EE spouses relapsed, although no patients living with low-EE spouses did so. The results replicate the association found by Vaughn & Leff between EE and depression, and suggest that the EE construct has predictive validity in both schizophrenic and depressed populations.

The course of psychiatric illness is an important issue. Whilst the aetiology of many psychiatric disorders remains unclear and thus precludes the use of primary prevention techniques, a solid understanding of the factors associated with psychiatric relapse is of evident value for intervention.

Among depressives, many factors have been suggested to be associated with relapse, including duration of the illness (Keller & Shapiro, 1981), age (Cadoret *et al*, 1980), marital disharmony (Kerr *et al*, 1974) and family levels of expressed emotion (EE) (Vaughn & Leff, 1976). Among these, EE is a particularly interesting variable since previous research has already established it to be reliably associated with relapse rates in schizophrenics (Brown *et al*, 1972; Vaughn & Leff, 1976; Vaughn *et al*, 1984). Moreover, within a schizophrenic population, it has been demonstrated that relapse rates can be influenced by interventions designed to reduce EE levels (Leff *et al*, 1982). Not only is EE therefore important, in that it may be of predictive utility in more than one psychiatric group, but it seems also to be modifiable and is thus of value in the prevention of psychiatric relapse.

In Vaughn & Leff's 1976 study, depressed patients living with relatives who made two or more critical remarks about them during interview, were significantly more likely to relapse over the course of a nine-month follow-up than patients living with low-EE or non-critical relatives. Since Vaughn & Leff's demonstration of the influence of EE in a depressed population was published in 1976, no reports of replication have appeared in the literature. However, additional investigations of the association between EE and the post-hospital course of depression are essential before it can be claimed that the construct has predictive validity for this group. One study has failed to find any significant association between EE and recovery (Goering *et al*, unpublished). However, since Keller & Shapiro (1981) in their follow-up study of depression found the predictors of recovery and relapse not to be the same, this lack of association is not altogether surprising.

The present study represents the first full replication of the work carried out by Vaughn & Leff (1976), and concerns the influence of EE levels on the relapse rates of married, depressed hospital in-patients. Based on the results of the earlier study, it was predicted that spouses' levels of EE would be significantly associated with outcome, and that depressed individuals would relapse at lower levels of spouse criticism than the levels typically found to be associated with relapse in schizophrenics.

Method

Patients were recruited while in a psychiatric hospital suffering from a major depressive episode. During this key hospital admission, their spouses were interviewed with the Camberwell family interview (CFI), and levels of EE were assessed. Both patients and spouses completed the Beck Depression Inventory (Beck *et al*, 1961) and the Dyadic Adjustment Scale (Spanier, 1976), a self-report measure of marital satisfaction.

After discharge from hospital with clinical improvement, all patients were followed-up for a period of nine months. During this time, they received two visits, and their psychiatric state was assessed on both occasions, to provide information about relapse.

Patients

Subjects were recruited from three psychiatric hospitals within a 25-mile radius of Oxford. All were required to be in-patients suffering from an episode of major depressive disorder which met both the Research Diagnostic Criteria (Spitzer *et al*, 1978) and the criteria of the Present State Examination (PSE; Wing *et al*, 1974). In addition, patients had to be married or currently living with a steady partner, and aged between 20 and 70 years. Individuals with suspected organic illness were excluded, as were those with delusions or hallucinations, since patients with these symptoms had not formed part of Vaughn & Leff's original study sample.

After interview with the PSE, patients' symptoms were evaluated using the CATEGO diagnostic computer programme (Wing & Sturt, 1978). Provided they were clinical cases of depression at ID level 5 or above on the PSE, and their reported symptoms also met the RDC, patients were considered acceptable for entry into the study.

A total of 42 patients met the above criteria and agreed to take part in the investigation. Over the course of the nine-month follow-up period, however, one patient withdrew from the study and a second suffered an episode of schizophrenia and was consequently removed from the group. One other patient who discharged himself from hospital against medical advice was also excluded from the sample. The data to be presented in this study are thus based on information collected on a total of 39 patients (16 men and 23 women) and their spouses. Due to time pressure, one spouse would only agree to be interviewed with the CFI for 25 minutes. During this time, he made three critical comments about his wife. Since he did not complete the full interview, he cannot always be classified as low or high-EE, and data from this individual are thus absent from some of the analyses.

The mean age of the patients in the sample was 47.6 (Table I). Couples had typically been married for about 22 years and had two children. The mean marital adjustment scores of both patients and spouses in the sample indicated a generally non-distressed population, which was middle- to working-class. While all levels of the social spectrum (as classified according to Goldthorpe & Hope, 1974) were represented, the mean social class of the couples was 19, which is reflective of such occupations as painter, carpenter, and publican.

TABLE I
Sample characteristics: patients and spouses

Variable	*Mean*	*SD*
Patients		
Age	47.6	12.1
Length of marriage	21.9	13.0
DAS	103.5	18.8
Beck	25.0	10.4
Social class*	19.4	11.1
Number of children	2.3	1.1
Spouses		
Age	47.9	12.3
DAS	104.3	16.7
Beck	5.7	3.8
Critical comments (EE)	8.3	5.8

$n = 39$ patients: 23♀ 16♂
*As assessed by Goldthorpe and Hope's (1974) classification scheme.

Reliability of psychiatric assessment

Two trained interviewers, a psychologist (JH) and a psychiatrist (JO), were responsible for the clinical assessment of patients at admission to the study. Levels of inter-rater agreement were high. In no instance was a patient identified as a psychiatric case by one rater and not another. Thus, the level of reliability of the PSE, calculated using the unit of data which was actually being used in the investigation (i.e., case vs non-case) was 100%. A more fine-grained investigation of the reliability of the PSE at the symptom level also gave encouraging results. Using very strict criteria of agreement (the same symptom had to be rated in exactly the same way by each rater) the inter-rater reliability, using audiotaped interviews, between the investigator and the principal psychiatrist was 98% ($n = 18$ tapes), while inter-rater agreement between these two raters and the third independent checker (also a psychiatrist) was 82% ($n = 5$ tapes). These results thus confirm that the PSE was being used reliably and that agreement levels between all three raters used was high.

Ratings of expressed emotion

All spouses were interviewed using the abbreviated form of the CFI (Vaughn & Leff, 1976b). Since previous research had suggested that the amount of criticism relatives make about depressed patients is linked to the length of interview (Vaughn & Leff, 1976b), only the critical comments made during the first hour of interview were used to assess levels of EE. Comments were coded as critical on the basis of content and voice tone by the first author, who had been appropriately trained. Inter-rater agreement between the investigator and a criterion rater at the Institute of Psychiatry was high after training ($r = 0.90$, $n = 12$ tapes) and remained so during the course of the study ($r = 0.091$, $n = 12$ tapes).

Relapse

All follow-up interviews were conducted by the second author, who was blind to the original levels of spouses' EE. Relapse assessments were made three months and nine months after patients had been discharged from hospital with clinical improvement. Improvement was always determined by the hospital clinician in charge of each case, and patients were discharged only when they were considered well enough to return home. The mean length of stay in hospital was 8.4 weeks (range 2–29 weeks); there was no significant relationship between the length of time a patient stayed in hospital and subsequent outcome.

At each follow-up visit, patients were interviewed using the PSE and were questioned about their psychiatric state and levels of functioning in the previous month. They were then asked about the period prior to this, in order to establish whether there had been an episode of depression in the intervening period. Two follow-up interviews were conducted over the nine months, in order to increase the reliability of the relapse data collected.

Patients were considered to have relapsed if they reported an episode of depression during follow-up which was accompanied by symptoms leading to them being

TABLE II

Demographic and clinical predictors of relapse

Measure	*Relapse (n=20)*	*No relapse (n=19)*	*t*	χ^2	*P*
Age	46.2 (12.2)	49.2 (12.0)	.76		>.1
Length of marriage	22.3 (13.7)	21.6 (12.6)	− .15		>.1
Social class	16.9 (11.2)	22.2 (10.5)	1.52		>.1
Number of children	2.2 (0.8)	2.4 (1.3)	.62		>.1
Number of symptoms on PSE	29.7 (7.7)	24.5 (8.9)	−1.86		.071
Beck score	28.3 (8.7)	21.6 (11.2)	−1.85		.074
PSE severity level	6.3 (0.8)	6.3 (0.7)	.00		>.1
Weeks in hospital	9.1 (6.4)	7.8 (5.2)	64		>.1
Sex	12♀ 8♂	11♀ 8♂		.02	>.1
Family history	12(−) 6(+)	7(−) 8(+)		1.34	>.1
Previous psychiatric treatment	4(−) 16(+)	9(−) 9(+)		3.78	.052

Note: All Chi-square statistics given are raw Chi-square values. In every instance where a significant result is reported, the corrected value is also significant.

classified as a case of depression at ID level 5 or above, using the CATEGO diagnostic computer programme. Readmissions to hospital were considered as relapses if patients met PSE criteria. The one exception to this concerned a patient who was readmitted with an episode of mania; this episode (which met PSE criteria for mania) was considered a relapse, since the patient was clearly not psychiatrically well during the follow-up period. All other instances of relapse, however, involved episodes of depression.

Results

Rates of relapse

Rates of relapse found in the present study are remarkably similar to those reported by Vaughn & Leff in their 1976 investigation. While in the earlier study 16 out of 30 patients relapsed during the follow-up period (a relapse rate of 53%), 20 of the 39 patients in present study relapsed, a relapse rate of 51%. Of the 20 patients who did relapse, seven (35%) were actually readmitted to hospital so that 18% of the total group were rehospitalised within nine months of discharge. This again compares favourably to the 23% overall readmission rate reported by Vaughn & Leff.

Demographic and clinical predictors of relapse

Within the group of demographic variables investigated (Table II), neither age, social class, nor length of marriage predicted relapse; sex of patient was also not a predictive factor. Clinical variables such as previous psychiatric treatment, family history of psychiatric difficulty, and duration of key episode (i.e. time spent in hospital) also failed to predict relapse, although the association between previous contact with psychiatric services and the probability of relapse just failed to reach the conventional alpha level of 0.05. Two other variables, the patients' total PSE symptom score and score on the BDI, were also slightly, but non-significantly related to relapse. Thus, none of the demographic or clinical variables investigated was a good indicator of relapse in the depressed patients studied.

The relation between EE and relapse

As predicted, levels of spouse criticism as assessed by CFI ratings were strongly associated with clinical relapse. While the mean number of critical comments made by spouses of non-relapsing patients was 6.1 (SD=5.7), the mean number of critical remarks made by the spouses of patients who relapsed was 10.5 (SD=5.2; $t=2.51$, $P<0.02$). Thus, spouses' EE is significantly associated with the relapse rates of depressed patients.

Tables III and IV show the relationship between EE and relapse rates, when several different cut-off points are used to designate spouses as high or low in EE. As can be seen from the first of these tables, there is a significant association between EE and relapse when a cut-off of two or more critical remarks is used to assign spouses to the high EE group. The data from the present study thus replicate the earlier findings of Vaughn & Leff and provide further support for the influence of EE on depressive outcome.

Within the present sample, however, the most clear separation of the relapse and no-relapse groups came when a cut-off of three critical remarks was employed. As Table III shows, none of the eight patients living with low-EE spouses relapsed, although 20 of the 31 patients (or 65%) living with high-EE spouses did so. Thus, while these data replicate the results of Vaughn & Leff, the optimum cut-off point in this study seems to be three rather than two critical remarks. The difference between the two different

TABLE III

Relation between spouses' criticism and patients' relapse

(a) Using a criticism threshold of two critical comments

	No relapse	*Relapse*	*% Relapse*
2+ Critical comments	14	20	59%
<2 Critical comments	5	0	0%
$\chi^2=6.04$			$P=.014$

(b) Using a criticism threshold of three critical comments

	No relapse	*Relapse*	*% Relapse*
3+ Critical comments	11	20	65%
<3 Critical comments	8	0	0%
$\chi^2=10.60$		0	$P=.001$

TABLE IV

Relation between spouses' criticism and rates of relapse

Criticism threshold		*% Relapse*	χ^2	*P*
4+ Critical comments	(18/28)	64%	5.80	<.02
<4 Critical comments	(2/10)	20%		
5+ Critical comments	(18/27)	67%	7.40	<.01
<5 Critical comments	(2/11)	18%		
6+ Critical comments	(15/23)	65%	3.70	.054
<6 Critical comments	(5/15)	33%		
7+ Critical comments	(14/22)	64%	2.54	.11
<7 Critical comments	(6/16)	38%		
8+ Critical comments	(13/19)	68%	3.80	.051
<8 Critical comments	(7/19)	37%		

cut-offs is minimal, however, and the findings confirm that depressed patients do relapse at lower levels of criticism than schizophrenics, for whom the most appropriate cutting-score is six (Vaughn & Leff, 1976) or seven (Brown *et al*, 1972) critical comments.

Although reducing the amount of face-to-face contact between patients and high-EE relatives can protect against relapse in schizophrenics, it does not seem to be a variable of importance in depressed populations. Vaughn & Leff's original work failed to find any relationship between the amount of contact between patients and relatives and patterns of relapse. In the present study, time spent in contact with a high-EE spouse (>2 or >3 critical comments) was also unrelated to relapse, either when analysed using the cut-off of 35 hours per week so important for schizophrenics, or when analysed by dividing the groups at the median of 49 hours per week. There was also no significant correlation between relapse and the number of hours per week patients and spouses typically spent together ($r=-0.12, P>0.1$).

The protective effects of continued medication in the depressed patients could not be investigated, owing to the fact that medication patterns in the patients studied were often erratic. Patients frequently changed medication, failed to take it as directed, or simply stopped taking it when they improved. Due to problems in collecting reliable data in this area, the effects of regular drug-taking on outcome are thus not evaluated.

One interesting finding within the present study concerns the lack of association between the number of symptoms reported by the patients and the number of critical remarks made by their spouses. Whereas Vaughn & Leff found a correlation of 0.48 between total symptom score of the patients and the frequency of criticisms made by relatives, there was no such significant correlation within the present study ($r=0.01, P>0.1$). It is therefore not clear whether attributes of patients are associated with criticism from a spouse. This is not to say that criticism necessarily arises *de novo*, however, and some suggestions for further research in this area have been made elsewhere (Hooley, 1985). However, at least within the present sample, the level of symptomatology reported by patients seems unrelated to the level of EE measured in the spouse.

Discussion

The above findings show that no demographic or clinical variables were predictive of relapse in the depressed population studied. As predicted, however, spouses' levels of EE were significantly associated with later psychiatric morbidity in the discharged patients; patients living with high-EE spouses had a poorer nine-month prognosis than those living with low-EE spouses. The results thus replicate the earlier work of Vaughn & Leff (1976) and suggest strongly that EE is a variable which is of predictive utility in both schizophrenic and depressed populations.

As expected, the present data also show that depressed patients tend to relapse at lower rates of criticism than schizophrenics. While Vaughn & Leff found the best separation of the relapse and the no-relapse groups came from using a cut-off of two or more critical comments to define high EE, and this cut-off was also associated with patients' relapse in the present study, the best separation within the current investigation was obtained when a cut-off of three or more critical comments was used. Both of these cut-points are well below those previously established as important in the prediction of relapse in schizophrenics, suggesting that depressed individuals may not have the same tolerance for criticism as individuals suffering from schizophrenia.

Why depressed patients should relapse at lower levels of criticism than schizophrenics is a question which remains unanswered. Vaughn & Leff (1976) have suggested that depressives are in some way more sensitive to criticism than schizophrenics, although the exact nature of this increased sensitivity was not specified. Precise data on this issue are lacking, but other findings from this sample (Hooley, 1984 unpublished) provide no evidence of increased sensitivity to negative spouse-behaviours on the part of the depressed. When patients were asked to rate videotaped recordings of interactions with their spouse, high-EE spouses were not rated any more negatively or less positively than low-EE spouses were rated by their depressed partners. Moreover, additional *post-hoc* analyses did not reveal patients who relapsed to be more aware of the negative aspects of their partners' behaviour than those who remained well. It is thus interesting to speculate whether the apparent sensitivity even to low levels of criticism demonstrated by depressed patients is in any way a function of who is doing the criticising. In other words, the explanation for the difference in thresholds to criticism found between schizophrenic and depressed groups may be less a reflection of diagnosis than of domestic situation. In all cases in the present study, and in all but two of the cases in Vaughn & Leff's (1976) study, depressed patients were living with and being criticised by spouses. The key relative of a schizophrenic patient, on the other hand, is equally likely to be a spouse or a parent.

The crucial issue may thus be associated with the source of the criticism—criticism from a spouse may simply be more salient and more distressing for a patient than criticism from a parent. There are several reasons for this. An obvious one concerns habituation to criticism from parents due to developmental history: perhaps people are used to such criticism and indeed expect their parents to highlight their faults and deficits. Second, and perhaps more important, is the probability of termination of the relationship. The parental bond is rarely broken and parents continue to be parents, irrespective of what their offspring do. The marital relationship in contrast is inherently much less stable, and unlike parents, spouses are much more likely to opt out of a relationship which is not satisfying to them.

Moreover, Jacobson *et al,* 1980, 1982) have suggested that distressed couples are more reactive to both positive and negative events than non-distressed couples, with negative events particularly having a different meaning for the former, as regards the way they process and interpret what happens within their relationships. Criticism from a spouse may thus have greater impact for patients within distressed marriages, although any criticism from a spouse may be more likely to be interpreted as reflecting dissatisfaction with the relationship generally, and consequently may lead to fears of possible termination. Relationships with parents, however, are quite different. While parents do, on occasion, dissociate themselves from their offspring, the rate with which they do this in no way approaches the rate at which couples divorce. Criticism from a spouse may thus be more disturbing for patients than criticism from a parent, since it is more likely to provoke feelings of insecurity and fears concerning possible loss of affection.

The overall quality of the marital relationship and the extent of the patient's dependence on this relationship may both be important. With respect to marital independence as a possible factor protecting against criticism from a spouse, it is interesting that in the present study, of the nine patients who failed to relapse despite living with very high-EE spouses (i.e., those who made seven or more critical remarks (mean = 11·2, range 7–20)) seven were men. Since the costs of ending a relationship, although significant for men, are still likely to be lower than for women (many of whom have no alternative source of financial support or marketable job-skills), it is possible that this may in some way offer them some protection against the influence of a high-EE wife.

Interestingly, the two women who had very high-EE spouses but nonetheless remained well were also relatively uncommitted to their marriages. One had steady employment which provided free housing and was in addition, having an affair with a fellow employee, while the second had left her husband on several occasions and for extended periods to either live on her own or with a number of male partners. In neither case could these women be considered maritally vulnerable, in the sense of being emotionally and financially dependent on their husbands. The effects of their husband's criticisms may thus have been reduced as a consequence of this.

Clearly, this hypothesis is still untested and cannot be investigated within the present study. However, a re-analysis of Vaughn & Leff's 1976 schizophrenia data might allow the optimum cut-off point for the schizophrenics living with parents to be compared to that of the schizophrenics living with spouses. While the mean optimum point for the group as a whole may be six or seven critical comments, a re-analysis might reveal a cut-off for the patients living with spouses that is much nearer the optimum for the depressed group. Reanalysis might also reveal that the optimal cut-off point for patients living with parents is even higher than the currently used threshold might suggest.

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Jill M. Hooley, BSc, DPhil, *Assistant Professor, Department of Psychology and Social Relations, Harvard University, Cambridge, Massachusetts, 02138*

John Orley, MA, BLitt, DM, MRCPsych, *Senior Medical Officer, Division of Mental Health, World Health Organization, Geneva*

John D. Teasdale, MA, PhD, *Senior Research Psychologist, Department of Psychiatry, University of Oxford, Warneford Hospital, Oxford*

*Correspondence

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Psycho-Social Predictors of Chronicity in Depressed Patients

R. M. A. HIRSCHFELD, G. L. KLERMAN, N. C. ANDREASEN, P. J. CLAYTON and M. B. KELLER

Nineteen patients with an episode of major depressive disorder who did not recover within two years of prospective follow-up were compared with an equal number who recovered within a year of the initial evaluation and remained well through the two-year follow-up date. The groups were individually matched for age, sex, primary/secondary status, and prior duration of episode. The only psycho-social variable that predicted chronicity was increased neuroticism on self-report personality inventories administered during the index evaluation. Early loss, recent life events, and recent social supports were not predictive of outcome.

Depression is usually thought to be an episodic disorder in which most patients recover and return to a pre-morbid state of well being. However recent work has challenged this long held clinical belief. Keller (1984), for example, found the rate of chronicity to be nearly 20% in patients with major depressive disorder. Since depression tends to strike individuals during their life period of maximum productivity, this issue is particularly disturbing. Prediction of chronicity is therefore of substantial public health concern.

The course of depressive illness is best predicted by previous clinical history. In a study of chronic depression, Keller (1984) found that the most powerful predictor of chronic course is long duration of the depressive episode prior to assessment and treatment. Conversely, the most powerful predictor of recovery is acuteness of onset (Keller, 1982).

In this paper, we examine psycho-social predictors of a chronic course in depressive illness. The question we ask is whether psycho-social variables contribute to the prediction of chronicity over and above the factor of prior duration of episode. Variables examined include socio-demographic characteristics, personality, life events, early life experience, and social supports.

Method

Subjects were selected from a sample of moderately to severely ill in- and outpatients with affective disorders who presented for treatment at one of five university medical centres participating in the Clinical Studies of the NIMH-Clinical Research Branch Collaborative Program on the Psychobiology of Depression ('Collaborative Study').

Assessments

All patients were evaluated with the Schedule for Affective Disorders and Schizophrenia (SADS), and other standardised evaluations (Endicott & Spitzer, 1978). Details of the intake and follow-up assessments and the overall goals and background of the research programme have been described previously (Katz *et al*, 1979; Katz & Klerman, 1979). Subjects were re-interviewed at six-month intervals, using the Longitudinal Interval Follow-up Evaluation (LIFE) (Shapiro & Keller 1979). Change points in psychiatric state were recorded by filling in week ratings of psychopathology for each disorder which the patient had at the time of entry into the study, and for conditions which developed subsequently.

All subjects received a comprehensive socio-demographic and personal background interview, the Personal History of Depressive Disorders (PHDD) (Larkin & Hirschfeld, 1977) and an interview on personal resources and social supports for the year prior to admission, the Personal Resources Inventory (PRI) (Clayton *et al*, 1977). Life events were assessed at the time of the subject's index evaluation by a trained interviewer, using a modification of the life events section of the Psychiatric Epidemiology Research Interview (PERI-M) (Hirschfeld *et al*, 1977). This interview recorded the occurrence of 110 life events in the year preceding admission to the study. Stress and distress ratings were derived for each subject, based on the system of weightings for life events developed by Tennant & Andrews (1976) and also on that developed by Holmes & Rahe (1967).

Subjects also received a Personality Battery composed of 436 items, measuring 17 substantive scales, drawn from five different self-report personality inventories. The scales, selected on the basis of their clinical or empirical relevance to affective disorders, include: seven scales from the Guilford-Zimmerman Temperament Survey (Guilford & Zimmerman, 1949); the Interpersonal Dependency Survey (Hirschfeld, 1977); the shortened version of the Lazare-Klerman-Armor Personality Inventory (Klerman *et al.*, 1977); the Maudsley Personality Inventory (Eysenck, 1962), and two sub-scales from the Minnesota Multiphasic Personality Inventory (Hathaway & McKinley, 1951).

Sample selection

Of 787 patients who entered the Collaborative Study with a diagnosis of Major Depressive Disorder, 234 were excluded because they were either bipolar or schizo affective, and a further 123 because they had a major depression superimposed on a chronic minor depression. Of the remaining 430, two-year follow-up data were available on 300. It was from this pool of 300 patients that we selected our study sample of chronic patients as well as our comparison group of patients who recovered fully.

Of the 300 patients available for study, 56 remained chronically ill throughout the entire two-year period—i.e. they did not have a period lasting at least eight weeks when they were free of symptoms of an affective disorder, or had only residual symptoms. Of the remaining non-chronic patients, 114 followed an episodic depressive course. This left 134 patients who fully recovered and remained well throughout the two-year follow-up evaluation. To be included in the 'recovered' group, however, patients had to be symptom-free or have had only minor residual symptoms for at least a year; this meant excluding from the analysis 17 patients who were recovered less than a year. We were therefore left with a very clean sample of 116 patients who recovered fully during the first year and remained well for the duration of the second year of follow-up.

A preliminary examination of the characteristics of the chronic and recovered patients revealed some striking differences in clinical features and history. As expected, recovered patients were more likely to have had an acute onset of illness. Almost one-third of recovered patients had an onset within four months of admission, as compared with only 6% of chronic patients. By contrast, one-third of chronic patients had been ill for more than two years prior to admission, as compared with 11% of recovered patients. The primary/secondary diagnosis was also found to predict chronic course in Keller's (1984) study.

In order to ensure that the psycho-social variables being studied were not influenced by known clinical differences between chronic and recovered patients, a matching design was adopted. Chronic and recovered patients were matched on prior duration of illness, and on primary/secondary sub-type.

Two additional matching variables—age and sex—were also included because of their known effect on psycho-social characteristics such as personality and life events. By matching our chronic and recovered groups on these variables, we could be reasonably confident that any psycho-social differences which we found between them were not related to prior duration of illness, or to primary/secondary sub-type.

Using this matching procedure, we were able to match 19 pairs of chronic and recovered patients (14 pairs of females and five pairs of males); 74% of patients were matched within nine years of age, while 26% were matched within 10 to 15 years. The mean age for chronic patients was 42.6 years, while that for recovered was 39.3 years. The mean difference in age was 3.3 years (±7.8). Matching on prior duration of episode was achieved within nine weeks for 68% of the sample, ten to 15 weeks for 27% and one pair (5%) was matched within 20 weeks. The mean prior duration of illness was 54.9 weeks for chronic patients and 53.7 weeks for recovered patients. The mean difference in prior duration of illness was 1.3 weeks (±9.1)

Thirty-two chronic patients could not be matched to recovered patients; in 80% of these cases, subjects could not be matched on prior duration of illness within four months. In 20% of cases, matches could not be found on age within 15 years, even though matches could be found on prior duration.

Sample characteristics

The chronic and recovered groups did not differ on most demographic and clinical characteristics including educational level, marital status, social class, number of children living at home, age at first hospitalisation, and overall severity of illness. Social functioning and overall functioning in the past five years were similar for both groups, as was total number of prior affective episodes. Chronic patients, however, had had more previous hospital admissions (Table I).

Statistical procedures

Personality scores were compared for chronic versus recovered patients, using the paired t-test. Based on findings by Weissman *et al* (1979) that chronic outcome was associated with higher neuroticism in depressed women, it was expected that chronic patients in our analysis sample would score higher than recovered patients in several personality measures related to neuroticism and general adjustment. As a test of the directional hypothesis, significance of the paired t-test for personality measures were assessed, using one-tailed probabilities.

To compare various stress and distress measures, however, a non-parametric test, the Wilcoxon Rank Sum Test, was used because of the skewness of the distribution of these scores. Demographic and clinical characteristics were compared using a chi-square or t-test, as appropriate, as were categories of life events.

Treatment data

Differences in clinical outcome may be the result of differences in treatment received, if the chronic patients received less adequate treatment overall than did the recovered patients. In order to examine this possibility, we sub-divided the somatic treatment received by all patients into four categories: intensive, moderate, low, and none. Intensive treatment refers to a course of ECT and/or, 200 mgs or more (or its equivalent) of a tricyclic antidepressant (or monoamine oxidase inhibitor) for at least four weeks. Moderate treatment refers to less than 200 mgs, but more than 125 mgs of the same for at least four weeks. Low treatment refers to less than 125 mgs, but more than 50 mgs of tricyclic antidepressant or its equivalent for a month. None refers to no somatic treatment at all or the equivalent of less than 50 mgs of antidepressant for any length of time.

Life events

Life events occurring within six months prior to admission

TABLE I

Clinical characteristics of chronic and recovered patients

		Chronic *(n=19)*	*Recovered* *(n=19)*	*Paired* *t-value*
Duration (in weeks) of current episode prior to entry into study	Mean	54.9	53.7	−1.82 NS
	(S.D.)	(29.5)	(29.4)	
Age at First RDC affective disorder	Mean	33.4	27.4	−1.73 NS
	(S.D.)	(14.2)	(10.4)	
Age at first hospital admission	Mean	36.5	35.0	−1.73 NS
	(S.D.)	(14.4)	(13.1)	
Extracted Hamilton[a]	Mean	29.5	28.3	−0.48 NS
	(S.D.)	(6.2)	(8.3)	
GAS[b] *Score (worst in week prior to admission)*	Mean	35.8	33.7	−0.48 NS
	(S.D.)	(11.3)	(15.5)	
Age	Mean	42.6	39.3	−1.82 NS
	(S.D.)	(13.4)	(12.7)	
Total Number of RDC affective episodes[c]				
1 (current)	*n*	5	4	*Chi-square*
	(%)	(26.0)	(21.0)	
2 or 3	*n*	10	11	−0.16
	(%)	(53.0)	(58.0)	
4 or more	*n*	4	4	
	(%)	(21.0)	(21.0)	
Number of psychiatric hospital admissions				
None	*n*	1	4	
	(%)	(6.0)	(24.0)	6.73 $P<0.05$
1 or 2	*n*	9	12	
	(%)	(52.0)	(71.0)	
3 or more	N	7	1	
	(%)	(41.0)	(6.0)	

[a] Endicott *et al* (1981)

[b] Global Assessment Scale (Endicott *et al* 1976)

[c] Excludes cases with missing information.

to the study were included in the analyses. Had the purpose been to ascertain aetiological information, life events occurring after onset or those confounded with depression would have had to be excluded. Since our purpose is to ascertain psycho-social predictors of chronicity useful to the clinician, we included all life events occurring within six months of admission to the study, which in most cases occurred after the onset of the illness.

Results

Personality

Thirteen of the 17 personality scales have been grouped into three constellations—Emotional Strength, Interpersonal Dependency, and Extraversion/Introversion. These constellations are based on the factorial structure of the scales and on their theoretical nature. The personality scores reported here were based on assessments made while the subjects were in the depressed state. We have shown previously that this state exerts a powerful influence on personality measures (Hirschfeld *et al*, 1983), and we do not therefore regard these scores as true reflections of pre-morbid personality.

Differences between chronic and recovered patients were found in the Emotional Strength constellation. Chronics had significantly higher scores on Neuroticism and lower scores on Ego Resiliency, while differences in Emotional Stability and Objectivity showed trends towards significance.

While these personality measures cannot be regarded as reflections of pre-morbid personality, neither are they

TABLE II

Index personality battery compared in chronic and recovered patients[a]

	Chronic		*Recovered*		*Paired t-value (1 tailed) probability)*
	Mean	*S.D.*	*Mean*	*S.D.*	
Emotional strength					
Neuroticism	36.8	(9.3)	29.5	(12.2)	−1.93 $P<0.05$
Emotional stability	9.6	(10.0)	13.6	(7.8)	1.66 $P=0.06$
Objectivity	12.4	(5.8)	14.8	(5.7)	1.66 $P=0.06$
Orality	9.5	(4.1)	8.2	(4.1)	−1.14 NS
Ego resiliency	15.5	(4.8)	19.2	(5.3)	3.04 $P<0.01$
Interpersonal dependency					
Emotional reliance on another person	47.5	(10.1)	50.9	(9.3)	1.31 NS
Lack of social self-confidence	38.9	(8.4)	36.2	(12.3)	−1.01 NS
Assertion of autonomy	302.0	(8.3)	28.2	(7.9)	−0.81 NS
Extraversion/Introversion					
Extraversion	20.5	(11.6)	21.4	(11.2)	0.55 NS
Sociability	14.5	(7.6)	16.3	(7.3)	0.86 NS
Restraint	18.4	(4.0)	18.8	(6.0)	0.27 NS
Thoughtfulness	18.5	(4.2)	17.4	(6.2)	−0.58 NS
Ego control	18.7	(4.7)	16.7	(5.6)	−1.25 NS
Miscellaneous					
General activity	16.1	(5.8)	17.2	(7.7)	0.63 NS
Ascendance	13.2	(5.9)	13.7	(6.1)	0.40 NS
Hysterical pattern	9.2	(3.3)	8.3	(4.1)	−0.79 NS
Obsessionality	13.2	(3.7)	12.1	(3.8)	−0.81 NS

[a]Using the t-test (1 tailed).
*$P<0.05$.
**$P<0.01$.
***$P<0.001$.

indicators of clinical severity. The severity of depression, as indicated by the Extracted Hamilton Score (Endicott *et al*, 1981), and the overall severity of psychopathology, as indicated by the Global Assessment Score (Endicott *et al*, 1976), were not different for the two groups, as we have already shown (see Table III). We also examined correlations between the personality scales and the measures of severity, and found no significant correlations.

Life events

There were no significant differences in the life events in the five months prior to admission (most of which occurred after onset of the index episode of major depressive disorder) (Table III). Scores on the Tennant Stress & Distress Scales and on the Holmes & Rahe Scale did not differ significantly. The large difference in the mean scores on the Holmes & Rahe Scale was not indicative of a significant difference, since a non-parametric test, the Wilcoxon Rank Sum Test, was used to compare the two groups, as described above. Among the 11 content categories of life events (school, work, love, health, crime and legal, money, birth, household, residence, personal, and death) no significant differences were found.

Early loss and social supports

Histories of early loss of a parent due to death separation or divorce were similar for the two groups.

The proportion of the recovered reporting high satisfaction with their principal role in life (i.e. outside work, domestic work, student) was four times that reported by the chronic group. This difference is statistically significantly. The two groups were similar with regard to adequacy of household finances, and with regard to 'count on' social support, both including and excluding mate.

Treatment

The two groups received almost identical amounts of treatment, as measured by category of somatic treatment.

TABLE III

*Life stress/distress experienced within six months of entry to the study compared in chronic and recovered patients**

		Chronic (n=19)	*Recovered (n=19)*
Measure of stress/distress			
Holmes & Rahe Score	Mean	100.7	58.3
	(S.D.)	(95.2)	(62.4)
Tennant Stress Score	Mean	21.8	22.8
	(S.D.)	(29.8)	(29.6)
Tennant Distress Score	Mean	17.1	16.2
	(S.D.)	(18.4)	(23.5)
Exit Events	Mean	0.3	0.2
	(S.D.)	(0.6)	(0.4)
Undesirable Events	Mean	2.7	1.1
	(S.D.)	(3.4)	(1.2)

*Using the Wilcoxon Rank Sum Test.

Among the chronic patients, ten received intensive treatment, five moderate treatment, two low treatment, and two none. Among the recovered patients, nine received intensive treatment, four moderate treatment, two low treatment, and four none. The chi-square for this is non-significant.

When the treatment was reviewed by individual case, the chronic group was found to have received much more intensive treatment. Six of the chronic patients received courses of ECT of at least seven treatments, and treatment with several forms of medication such as anti-psychotics or lithium was quite common. By contrast, the recovered group included only one patient with a course of ECT and no patients with a combination of MAO and tricyclic anti-depressants. An example of the treatment received by a chronic patient included a course of 12 ECTs, followed by 12 weeks of desipramine of 150 mgs a day plus nardil 45 mgs a day.

Therefore, the difference in clinical outcome clearly cannot be accounted for by a difference in treatment received by the two groups, because if anything, the chronic group received more intensive somatic treatment.

Discussion

Our results will be discussed by comparing them with previous reports on the relationship between psychosocial variables and chronicity in depressive disorders. Differing definitions of chronicity, as well as those of other variables, sometimes makes comparisons difficult; nonetheless, considerable consistency becomes apparent. We also discuss how factors such as diagnosis influence the interaction of psycho-social variables and chronicity.

Socio-demographic

We did not find that social class or financial resources predicted chronicity. However, the effect of age and sex could not be tested because we matched on these variables. In sharp contrast, Brown & Harris (1978) reported that chronicity was five times more prevalent among the working class women, compared with middle class women, in their community sample in Camberwell, London. Other investigators, however, did not find class differences associated with chronicity or with psychiatric disorders (Bebbington *et al*, 1981).

One possible reason for Brown & Harris' finding is that their 'working' class sample included many women living barely at subsistence levels in tenements with hopelessly inadequate sanitation and living conditions. The abject misery of ordinary life there may well have contributed to chronicity in this sample. Thus, chronicity may be associated with the lowest social class, but no relationship exists between chronicity and social class, one social class increases beyond that level.

Personality

The only relatively strong predictors of chronicity in our sample were certain personality measures, assessed when the patient was still somewhat symptomatic. Chronic patients were characterised as being more 'thin-skinned', and more likely to break under stressful conditions.

These assessments were performed after the acute symptoms of the episode had somewhat abated, but subjects were clearly not symptom-free. The clinical depressed state exerts a powerful influence on the assessment of personality qualities (Hirschfeld *et al*, 1983), compared with assessments made during truly asymptomatic periods. When comparisons of ratings are made on the *same patient* at a truly symptomfree point, as well as when there is evidence of depressive symptomatology, the ratings made in the depressive period show a substantial decrease in emotional strength, a substantial increase in interpersonal dependency, and a modest decrease in extraversion.

Therefore, we cannot assume that the index personality assessments necessarily reflect pre-morbid personality. On the other hand, differences on these personality measures cannot be attributed to differences in severity of depression, because the two groups did not differ on clinical severity. Perhaps the personality differences between the two groups that were assessed during the episode are exaggerations of pre-morbid differences.

These findings corroborate those of Weissman *et al* (1979), who found that the Maudsley neuroticism score predicted chronic outcome in 150 depressed women who were followed for up to four years after the acute episode. No other variable in that study was predictive of chronic outcome in this sample including age, race, social class, marital status, religion, number of previous depressions or suicide attempts, diagnosis, history of early deaths or separation from significant others, history of neurotic traits as a child, amount or type of stress in the six months before onset, and severity in pattern of pre-treatment symptoms.

Life events

We found very few differences in life events between the two groups in the period after onset of the disorder but prior to admission to the study. These findings contrast with those of Brown & Harris (1978), who reported that 28% of the women with chronic depression had a major housing problem, as opposed to only 1% of those with acute-onset depressions. Substantial differences in definition and assessment methods exist between the Brown & Harris sample and ours. They defined chronicity retrospectively, in terms of a subject having had a psychiatric disorder continuously for at least one year prior to the interview. We defined chronicity prospectively by the subject having experienced continuous depression for two years from the intake interview. Brown & Harris obtained their sample randomly from the community, whereas ours was entirely a psychiatric clinical sample. The issue of social class has been discussed above. Brown & Harris, therefore, have identified a group of working-class women in difficult social situations who are suffering from chronic psychiatric disorders. We, on the other hand, have identified a group of male and female psychiatric patients who have not recovered from their major depressive disorder within two years after entry into our study, in spite of treatment.

Implications

Clinical understanding of chronic depressions has become increasingly important in recent decades. There are at least two pathways to chronicity. One major pathway is that described in this study, namely patients with episodes of depression who fail to recover.

In addition, Klerman (1980), Akiskal (1983), and others have identified the important role played by dysthymia among the group of chronic depressions. Epidemiological studies (Boyd & Weissman, 1981) indicate that about 4% of the adult population meet the criteria for DMS-III dysthymia. In many of these patients, the onset occurred in adolescence and young adulthood with chronic impairments of self-esteem, depressive symptoms, and bodily complaints, and they are often diagnosed as having a personality disorder or 'characterological depression'.

The combination of these two pathways results in a high prevalence of chronic depression, which is increasingly of concern for community mental health services, psychiatric practice, and prevention.

As risk factors for chronicity are identified and confirmed, clinicians treating patients with acute depressive episodes will be in a better position to identify sub-groups most at risk for chronicity. It is to be hoped that intensive and vigorous treatment with both drugs and psychotherapy can avert chronic outcomes in many of these cases.

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*R. M. A. Hirschfeld, MD, *Chief, Affective and Anxiety Disorders Research Branch, Division of Clinical Research Branch, National Institute of Mental Health, Rockville, Maryland 20857, USA.*

G. L. Klerman, MD, *Professor of Psychiatry, Associate Chairman for Research, Cornell University Medical College, New York, N.Y., USA.*

N. C. Andreasen, MD. PhD, *Professor of Psychiatry, College of Medicine, University of Iowa, Iowa City, Iowa, USA.*

P. J. Clayton, MD, *Head, Department of Psychiatry, University of Minnesota, University Hospital, Minneapolis, Minnesota, USA.*

M. B. Keller, MD, *Assistant Professor of Psychiatry, Harvard Medical School and Director of General Psychiatry Practice, Massachusetts General Hospital, Boston, Massachusetts, USA.*

*Correspondence

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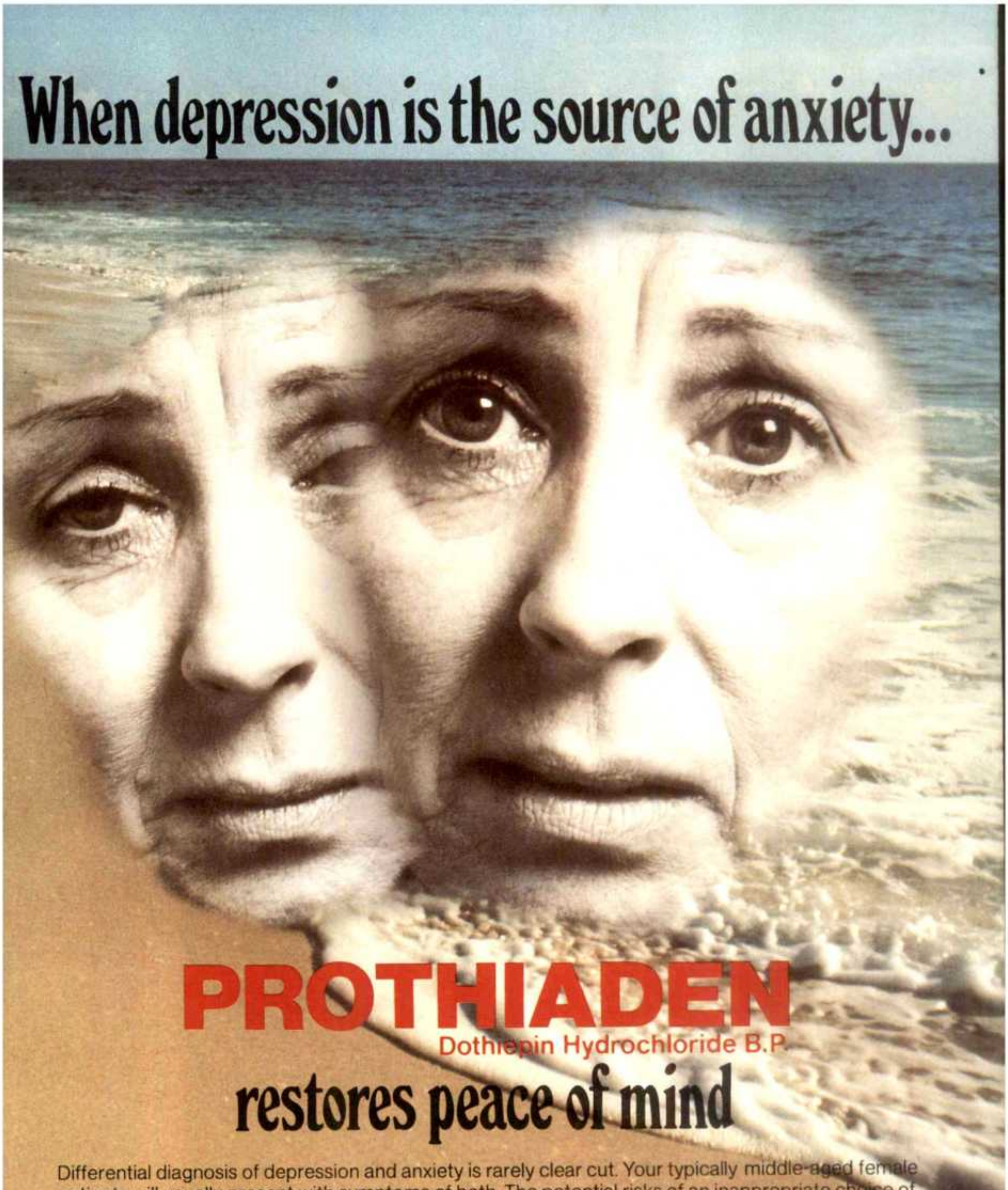
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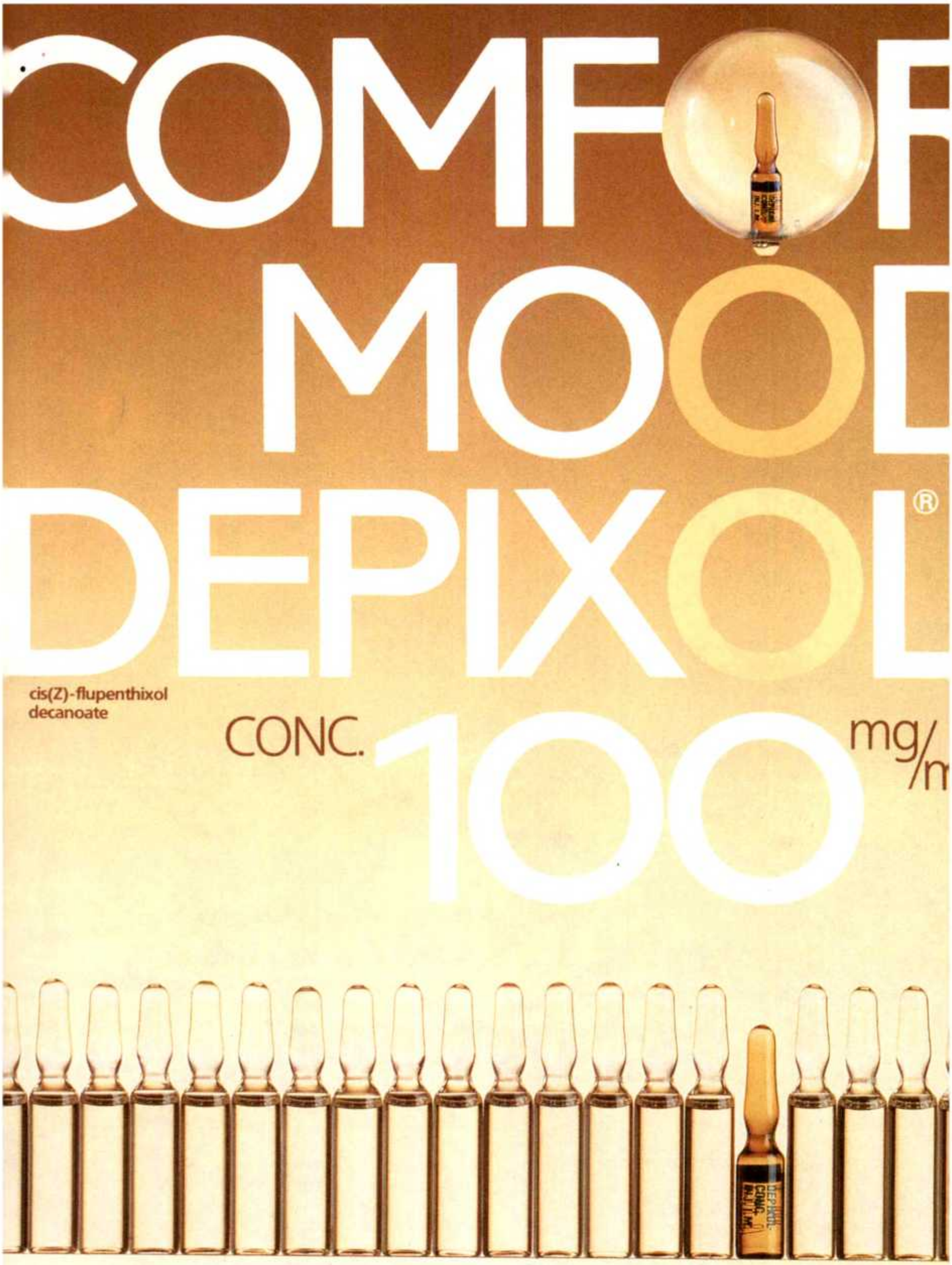
Presentation: Prothiaden is Dothiepin Hydrochloride B.P., an antidepressant of the tricyclic group. It is available as 25mg capsules and 75mg tablets. **Uses:** Prothiaden is indicated in the treatment of depression and associated anxiety. **Dosage:** Prothiaden should be given in a dosage of 75 to 150mg daily, based on response and severity. This may be taken as a single evening dose. In certain circumstances, i.e. in hospital use, Prothiaden has been given in dosages up to 225mg daily. Elderly – half the normal adult dose may be sufficient. **Precautions and Contra-indications:** Prothiaden has anticholinergic properties, therefore, it may precipitate urinary retention in susceptible individuals and its use should be avoided in patients with existing or potential urinary retention. Prothiaden should not be used in patients with closed-angle glaucoma. Caution is advised when treating epileptic patients and those with cardiovascular disorders. Prothiaden should not be used with MAO inhibitors nor within 14 days of ceasing such treatment. It may modify the action of some CNS depressants, catecholamines and hypotensive agents. **Side Effects:** These are usually mild and normally controlled by reducing the dosage. The following have been reported: dryness of mouth, constipation, disturbed accommodation, orthostatic hypotension, palpitations, somnolence, tremor, headache. **Basic N.H.S. Price:** 28 x 75mg £3.73. **Product Licence Numbers:** PL0014/5941, PL0014/0209. ® The Boots Company PLC, Nottingham, England. Further information available on request.



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reduction or anti-Parkinson drug treatment. **Contra-indications** Not recommended for overactive patients, or for those with Parkinsonism, severe arteriosclerosis, senile confusional, or advanced renal, hepatic, or cardiovascular disease, intolerence to other neuroleptics, pregnancy. **Package Quantities** Boxes of 10 x 20mg (1ml), 10 x 40mg (2ml) 10 x 100mg (1ml) ampoules; 5 x 20mg and 5 x 40mg syringes; 1 x 200mg (10ml) and 1 x 500mg (5ml) vials. **Further information**

cholinergic anti-Parkinson drugs if extrapyramidal symptoms occur. (b) By sedation (with benzodiazepines) in the unlikely event of agitation or excitement. (c) By noradrenaline in saline intravenous drip if the patient is shocked. **Basic NHS Cost** 10 x 20mg amps £15.53; 10 x 40mg amps £25.99; 10 x 100mg amps £59.53; 5 x 20mg syringes £8.51; 5 x 40mg syringes £13.74; 200mg (10ml) vial £14.74; 500mg (5ml) vial £28.27. (Prices correct at time of printing.)

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Prevalence of the Fragile X Syndrome in an Institution for the Mentally Handicapped

DAVID A. PRIMROSE, RABIA EL-MATMATI, ELIZABETH BOYD, CHRISTINE GOSDEN
and MARJORIE NEWTON

In an investigation to find the prevalence of the fragile X (Martin Bell) syndrome in a mental handicap hospital, chromosomal investigations were carried out in 196 males selected out of a total of 512, and also in 20 female patients who were related to some of the selected males. Fragile X cells were found in 41 of the males and two of the females; in 21 of the males it was associated with macro-orchidism. The overall prevalence in the hospital for males (8.0%) ranks this syndrome next in importance to Down's syndrome as a known cause for mental handicap.

The fragile X (Martin Bell) syndrome (Martin & Bell, 1943; Richards & Webb, 1982) of X-linked mental handicap is an important cause of mental handicap in males. The condition, recently reviewed by Turner & Jacobs (1983), is characterised by moderate to severe non-specific mental handicap often accompanied by macro-orchidism. It is associated with the presence, in a percentage of lymphocytes cultured under appropriate conditions, of a fragile site on the long arm of the X chromosome (Xq27).

Though many aspects of the fragile X syndrome are currently under intense research (Opitz & Sutherland, 1984), there are to date comparatively few estimates of its frequency in institutions for the mentally handicapped. The problem has been approached in several ways. Three studies (Sutherland, 1982; Froster–Iskenius *et al*, 1983; Jacobs *et al*, 1983) reported cytogenetic screening of all male patients in an institution for the mentally handicapped, while two others (Nielsen *et al*, 1982; Howard-Peebles & Finley, 1983) first screened for macro-orchidism and then carried out chromosome analysis in individuals found to have large testes. Others have estimated the frequency of the syndrome by studying pairs of retarded brothers (Fishburn *et al*, 1983) or by screening all male children with mental handicap of unknown aetiology from a population (Blomquist *et al*, 1982).

We have used a combination of these methods to estimate the frequency of the fragile X syndrome in a large hospital for the mentally handicapped.

Method

(a) Random group

There are just over 500 adult males in the hospital; chromosome analysis for fragile X status was carried out on 100 of them. Lymphocyte cultures were prepared using TC199 containing methotrexate and 50 cells stained with Leishmann from each individual were analysed for the fragile X. The men were selected so that approximately

TABLE I
Occurrence of fragile X in unselected series (n = 100)

Patient	*IQ*	*Right testis (ml)*	*Left testis (ml)*	*% fra(X) +ve cells*
1	44	35	35	42
2	75	25	25	2
3	<30	30	30	32
4	<30	20	20	28
5	57	10	10	4
6	30	hydrocoele	25	28
7	<30	20	20	4

TABLE II
Occurrence of fragile X in group selected for macro-orchidism (n = 30)

Patient	*IQ*	*Right testis (ml)*	*Left testis (ml)*	*% fra(X) +ve cells*
8	<30	50	50	38
9	48	50	50	36
10	<30	50	40	35
11	34	50	35	10
12	45	40	35	16
13	30	50	50	24
14	45	50	40	6
15	30	35	30	16

half had an IQ below 50 (admission to hospital is biased in favour of those who are more severely handicapped). Those persons (112) who already had a known cause of their mental handicap were excluded, i.e. Down's syndrome (65) cerebral palsy (32), and those with a genetic or chromosomal abnormality (15), including the fragile X (8). Apart from these limitations, the individuals were selected at random and seven were found to have the fragile X chromosome (Table I). Of these, four had an IQ of 30 or below and for the other three, the IQs were 44, 57, and 75.

(b) Group with macro-orchidism

Testicular volume of the 512 adult males was measured by means of comparison with a series of plastic ellipsoids of standard volume. There were 61 of the adult males with at least one testicle of volume 35 ml or greater; 13 of these were in Group (a) and 17 in Group (c), leaving 31 unexamined for fragile X. Blood from 30 of these was examined, and eight were found to have fragile X cells (Table II). Of these, four had an IQ of 30 or below and for the other four, the results were 34, 45, 45, and 48.

(c) Family group

This group comprised 52 families in which there was a mentally handicapped patient as well as another mentally handicapped relative of either sex, represented in the hospital by 70 male and 20 female patients. Of the families, 49 had at least one mentally handicapped male, while in the other three families, there were no known male relatives.

The study of the random group, which preceded the family studies, had already tested three of the males, including two brothers, and these are included here. This group included three males with Down's syndrome, two brothers with epiloia, and a brother and sister with gangliosidosis (GM1), all of whom proved to be negative for fragile X. Fragile X was found in 24 of the males and two of the females, representing 16 of the families. These results are summarised in Table III, which also indicates IQ levels and the relationship with macro-orchidism.

TABLE III

Occurrence of fragile X in 52 families with more than one mentally handicapped member (n = 90)

Number of patients from 52 families	70 male	20 female
Number of patients found with fra X	24 male	2 female
Number of families with fra X	16	
Percentage distribution of fra X cells related to macro-orchidism and IQ		
Present in 20% or more of cells (nine have macro-orchidism; one with 42% has IQ 50, while others have IQ 30 or less)	11 patients	
Present in 5–10% of cells (one has macro-orchidism; all have IQ below 30)	4 patients	
Present in less than 5% of cells (two have macro-orchidism; two have IQ 30 and 32 and IQ range is from 46–62 for the other seven)	9 patients	
Total	24 patients	
Female patients		
1 20% of cells IQ 46		
2 20% of cells IQ 32		

Discussion

The random group studied here shows 7% of fragile X positive males. This figure is higher than that found in two other studies, one by Sutherland (1982), who analysed 444 institutionalised males with otherwise normal chromosomes, and found an incidence of 1.5% fragile X positive; and the other by Jacobs *et al* (1983), who in a study of 274 mentally retarded males on community placement found 1.8% to have fragile X cells. It compares, however, with the results of Froster–Iskenius *et al* (1983) who examined 242 institutionalised males with severe mental retardation and found 6.2% positive for fragile X. A similar figure of 6% was found by Blomquist *et al* (1982) in an unselected series of 96 severely mentally handicapped boys in a northern Swedish county.

In the group of patients selected for macro-orchidism (testis > 35 ml), the prevalence of fragile X was 27%. In a Danish study, Nielsen *et al* (1982) found no fragile X positive males among a group of 41 with testes of approximately 25 ml, but two of 11 with definite macro-orchidism were positive. Howard–Peebles & Finley (1983) also found a frequency of 27% fragile X positive males in those selected for macro-orchidism from the white male population of an institution for the mentally retarded.

In the family group, fragile X was found in 16 out of the 52 families (31%): of the 70 male and 20 female patients representing these families, fragile X cells were found in 24 of the males (35%) and two of the females (10%). Macro-orchidism was present in 12 of the males (50%) and tended to be associated with a higher proportion of fragile X cells. There was also a tendency for those with a higher proportion of fragile X cells to be more severely mentally handicapped. However, one of four brothers with fragile X in 42% of cells and gross macro-orchidism had an IQ of 50, whereas his three brothers with 52%, 28% and 26% positive cells all had IQ results of less than 30. Of two females, one is the sister of an affected male patient and the other is the maternal niece of an affected male patient.

Following on the above, blood from nine further patients who had prominent ears was examined, because this feature has also been described in fragile X, and two further cases were found. One patient with enlarged ears and testicular volume R/L: 30/30 ml is negative for fragile X, but has a deletion at Xq28.

The cumulative result of the above is that fragile X was found in 41 out of 205 males selected from a total of 512 (8.0%), and in two out of 20 selected female patients in a hospital for the mentally handicapped. Of the 512 males, 61 have macro-orchidism and, on examination for fragile X, it was found in 21 out of the 60 who were tested.

There was a tendency for those with a high proportion of fragile X cells to have more severe mental handicap, but as severe mental handicap is an important factor in admission to hospital, the relationship may not be a causal one. Where possible, IQ tests were performed using the Stanford-Binet, Form L-M, and comparison was made with results obtained (usually on the then current Stanford-Binet Modification) around the time of admission to hospital. No early result was available for one of the patients; 21 of the others had an IQ below 30 on admission and it is still below IQ 30. Of the others, 10 show a significant IQ deterioration with inter-test periods of from 18 to 35 years, six show no significant IQ change over inter-test periods of from 7–31 years, and three have shown significant improvement in IQ levels since admission (inter-test periods 11–39 years).

One of the males has schizophrenia. It is not considered that any of the patients is autistic, and although some are mute, good eye contact can be obtained with all of them.

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David A. Primrose, MD, FRCPsych, FRCP(G), *Consultant Psychiatrist and Physician Superintendent, Royal Scottish National Hospital, Larbert, Scotland FK5 4EJ* (retired 31 December 1984).

Rabia El-Matmati, MSc, *Research Student, Duncan Guthrie Institute of Medical Genetics, Glasgow.*

*Elizabeth Boyd, BSc, PhD, *Principal Cytogeneticist, Duncan Guthrie Institute of Medical Genetics, Glasgow.*

Christine Gosden, BSc, PhD, *Member of the Scientific Staff, MRC Clinical and Population Cytogenetics Unit, Edinburgh and Honorary Senior Lecturer in Human Genetics, King's College Hospital, London SE5 9RS.*

Marjorie Newton, MB, ChB, DObst RCOG, *Member of the Scientific Staff of the MRC Clinical and Population Cytogenetics Unit, Edinburgh.*

*Correspondence

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A Comparison of Drug-Related Problems in London Accident and Emergency Departments 1975–1982

HAMID GHODSE, JOHN STAPLETON, GRIFFITH EDWARDS, THOMAS BEWLEY and MUHAMMAD AL-SAMARRAI

Drug-related incidents dealt with by ten Accident and Emergency departments in Greater London during July 1982 were compared with those obtained from an identical survey in 1975. The number of incidents remained high, but there was a significant reduction in them and in the number of drug dependent attenders, compared with 1975: hynotic drugs were used in a significantly smaller percentage of drug overdoses, but there was increased use of minor tranquillisers. The possibility of using A & E departments to monitor drug misuse on a Regional basis is discussed.

The usefulness of Accident and Emergency (A & E) departments in monitoring drug-related problems is well established, both in the UK and internationally (Ghodse, 1976; Sivner & Goldberg, 1978; Hadden, 1978; Russe & Wells, 1980; Sellers *et al*, 1981; Ghodse *et al*, 1981). In the USA, the Drug Abuse Warning Network (DAWN) has been collecting information on a continuous basis since 1972 from hospital emergency rooms (and medical examiners) in 26 Metropolitan areas. The objectives of this system include the monitoring of drug abuse patterns and trends, assessment of associated health hazards, and provision of data for both local and international drug abuse policy and programme planning (National Institute on Drug Abuse, NIDA, 1983).

In the UK, despite expressed concern about drug misuse, there is no machinery for countrywide monitoring, apart from the statutory obligation of doctors to notify the Home Office of those who are dependent on certain controlled drugs in Class A. The London Casualty Survey, carried out in 62 hospitals in Greater London in July 1975 to monitor all patients presenting with drug-related problems, provided a methodology that could easily be incorporated into the routine of the busiest Accident and Emergency department. It permits repeated or continuous surveys (Ghodse, 1976), and has been selected and recommended by WHO as part of a drug abuse monitoring programme (Idanpaan-Heikkila & Khan, 1982); ten countries are currently conducting the survey using this method. In the UK, the study was repeated in ten hospitals in July, 1982, and the results compared with those obtained from the same hospitals, seven years previously.

Method

Full details of the method of the survey have been given elsewhere (Ghodse 1976): a specially designed questionnaire was completed for each patient who attended the A & E departments of the ten participating hospitals for the treatment of a drug-related problem. This recorded the age and sex of the patient, the drug of abuse and/or self-poisoning, and the source of supply. Casualty officers were also asked to assess the dependence status of the patient, in terms of defined criteria, and to identify the reason for the attendance, e.g. drug overdose, other reasons related to drug misuse (complications of self-injection, drug-induced psychosis etc.), or a demand for drugs.

Results

Numbers and rates

During the months of the 1975 survey, 474 of the 37,923 incidents dealt with in the ten A & E departments were drug-related, while in 1982, 412 of the 38,432 incidents were drug-related. The rate of drug-related attendances in the casualty population was therefore 12.5 per 1,000 in 1975 and significantly less, at 10.7 per 1,000, in 1982 ($x^2=5.1$; $P<0.025$). Excluding children under the age of 15 (who constituted approximately 43% of casualty attendances, but only 13% of the drug-related attendances) from any further statistical considerations, the rate of drug-related attendances in the casualty population was 20.1 per 1,000 in 1975, whereas by 1982, it had dropped significantly to 15.4 per 1,000 ($x^2=14.03$; $P<0.001$). The combined catchment population of the hospitals was approximately 1,374,500 in 1975 and 1,286,250 in 1982, giving monthly incidence rates for drug-related problems of 0.32 per 1,000 in 1975 and significantly less, at 0.26 per 1,000, in 1982 ($x^2=6.8$; $P<0.01$). Applying these monthly rates to the whole year gives equivalent yearly incidence rates of 3.8 per 1,000 in 1975, and 3.1 per 1,000 in 1982.

Excluding the children, there were 435 drug-related incidents during the study period in 1975, and 337 incidents in the corresponding period of 1982. In 1975, 413 incidents (95%) were of self-poisoning and 22 (5%) were attendances for other reasons such as the complications of self-injection, whereas in 1982, there were 311 (92%) cases of self-poisoning and 26 (8%) attendances for other reasons; these differences were not statistically significant ($x^2 = 2.3$; NS.

Sex

In both 1975 and 1982, 47% of patients with drug-related problems were male and 53% female; the sex was not recorded in one case in 1975 and in two cases in 1982.

Age

Table I shows the age-structure of drug-related incidents in the two periods of survey: the minor differences between 1975 and 1982 in the overall distributions were not significantly different ($x^2 = 8.4$; NS). In 1975, about 60% of incidents concerned people under the age of 30, whereas in 1982, the figure was 56%: this is reflected in the overall mean ages in the two groups, which was 31 years in 1975 and 32.5 years in 1982 ($t = 1.46$; NS). When comparing the age-distribution for males and females separately, the percentage of females in the under-30 age-group was somewhat higher in 1975 (63%) than in 1982 (53%). The reverse was the case for the males; 57% were under the age of 30 in 1975 and 59% in 1982. This trend towards an older female group was reflected in a significantly different mean age of females in 1975 (29.5 years) from 1982 (33 years) $t = 2.43$; $P < 0.02$).

Drugs and their sources

Table II shows the drugs used in incidents of self-poisoning in 1975 and 1982; it can be seen that the use of barbiturates decreased dramatically over this period, with 27% of cases taking them in 1975 and only 7% in 1982. The use of non-barbiturate hypnotics also fell significantly. In terms of the actual number of overdoses, self-poisoning with minor tranquillisers and non-barbiturate hypnotics showed little change between 1975 and 1982; the statistically significant increase in the percentage of incidents related to these drugs is due to the reduction in overdoses of barbiturate and non-barbiturate hypnotics.

Barbiturates were the only drug group which showed a significant change in their source of supply: in 1975, 38% whose source was identified had been obtained from GPs and 63% from hospitals, whereas in 1982, only 10% had been obtained from GPs ($x^2 = 5.1$; $P < 0.025$). A clearer picture of prescribing emerges if these percentages are also presented in numerical terms; thus GP-prescribed barbiturates accounted for 31 incidents in 1975, but only for two in 1982.

Poly-drug overdose

More than one drug was taken in 186 (47%) overdose incidents in 1975 and in 135 (45%) incidents in 1982. The mean number of drugs taken remained constant at 1.6 per person.

Previous overdoses

It was possible to ascertain whether the patient had taken an overdose during the previous year in 301 cases (73%) in

TABLE I

Age of patients attending with drug-related problems in 1975 and 1982

Age (yrs)	*1975*				*1982*			
	Male No.	*Female No.*	*Total No.*	*Total %*	*Male No.*	*Female No.*	*Total No.*	*Total (%)*
15–19	17	55	72	(18)	16	32	48	(15)
20–29	90	80	171*	(42)	70	60	130	(41)
30–39	37	37	74	(18)	29	30	59	(18)
40–59	33	34	67	(17)	22	37	59	(18)
60+	12	8	20	(5)	10	14	24	(8)
Total known	189	214	404	(93)	147	173	320	(95)
Not known	14	17	31	(7)	10	5	17*	(5)
Total	203	231	435	(100)	157	178	337	(100)

Percentages for age groups are based on known cases only.
*Numbers do not sum to the total as the sex of three patients was not known.

TABLE II

Agent of self-poisoning

Drug	*1975* No.	*1975* (%)	*1982* No.	*1982* (%)	*Significance of difference*
Barbiturates	106	(27)	22	(7)	$x^2=43.6, P<0.001$
Minor tranquillisers	111	(28)	115	(38)	$x^2=7.9, P<0.05$
Aspirin/codeine	85	(22)	86	(29)	$x^2=4.5, P<0.05$
Alcohol	103	(26)	88	(29)	NS
Non-barbiturate hypnotics	69	(18)	12	(4)	$x^2=30.3, P<0.001$
Anti-convulsants and Non-psychoactive drugs	37	(9)	63	(21)	$x^2=18.5, P<0.001$
Total incidents where drugs known	393	(95)	300	(96)	
Incidents where drugs not known	20	(5)	11	(4)	
Total self-poisoning incidents	413	(100)	311	(100)	

Percentages of each drug are based on the total number of incidents where the drugs were identified.
Percentages sum to more than 100% due to polydrug use.
There was no significant difference between 1975 and 1982 in the number of incidents in which anti-depressants, major tranquillisers, heroin, methadone, cocaine, amphetamines and other stimulants, hallucinogens, and gas/toxic agents, were used.

1975 and in 217 cases (70%) in 1982. In 1975, 133 patients (44%) had taken an overdose during this time whilst in 1982, this figure dropped significantly to 32% (69 cases) ($x^2=8.1$; $P<0.005$). This reduction was evident among both males and females separately, although more pronounced among males. The number of individuals who overdosed repeatedly (4 or more overdoses during the previous 12 months) also fell from 57 (19%) in 1975 to 19 (9%) in 1982.

Dependence

The dependence status of the patients was identified in 365 cases (84%) in 1975 and in 290 cases (86%) in 1982. In 1975, 141 (39%) patients were classified as definitely or probably drug dependent, whereas in 1982, this figure dropped to 75 (26%), ($x^2=11.9$; $P<0.001$). Although this pattern was apparent in both sexes, it was far more evident among females, where the reduction was from 56 cases (29%) to 21 (14%), ($x^2=11.6$; $P<0.001$), than amongst males, where the number of cases fell from 85 (50%) to 54 (41%), ($x^2=2.8$; NS).

Nature of overdose

The underlying nature of the overdose was identified in 341 cases (83%) in 1975 and in 267 cases (86%) in 1982, and differed significantly in the two surveys ($x^2=15$; $P<0.001$). In 1975, 72 overdoses (21%) were taken accidentally in the course of addiction, whereas in 1982 this figure had fallen to 27 (10%). This was compensated for by a higher proportion of suicidal attempts and of accidental overdose. The pattern is similar for male and females separately.

Other reasons for attendance

In 22 cases (5%) during the 1975 survey, casualty attendance was not a result of drug overdose. Of these, six (27%) made an attempt to obtain drugs and nine (41%) had infective complications of self-injection. In 1982, there were 26 (8%) similar cases, and the reasons for attendances were not significantly different, with eight (31%) attempting to obtain drugs, and 13 (50%) having complications of self-injection.

Disposal of patients

The disposal of patients was recorded in 94% of cases in both surveys. The pattern remained very stable, with about 65% being admitted to hospital in both surveys and 35% leaving after outpatient treatment (8% against medical advice). In the 1975 survey, two patients died in A & E departments, but during the 1982 survey, there were no deaths in the departments.

Discussion

The reduction in the number of drug-related problems seen in A & E departments in 1982, compared with 1975, is important, because it represents a true reduction in the incidence of problems serious enough to warrant urgent hospital treatment in the catchment area population. This seems to be due to a decrease in the misuse of all types of hypnotic drugs, both barbiturate and non-barbiturate. The dangers of barbiturates have long been recognised and since 1965, there has been a steady fall in the number of prescriptions issued for them. The Campaign on the Use and Restriction of Barbiturates (CURB) was launched in 1975 to accelerate this trend, and the results reported here can be interpreted as further evidence of the reduced availability of barbiturates (Bennett, 1981). The decrease in the number of drug-dependent individuals attending, and in those taking repeated overdoses during the previous year is probably also related to the reduced misuse of barbiturates. Since January 1st 1985, barbiturates (except phenobarbitone) have been added to the list of drugs controlled under The Misuse of Drugs Act 1971, and this is likely to reduce their availability still further.

A reduction in the use of one psychotropic drug by a population is usually associated with an increase in the use of another. Indeed, the reduced prescription of barbiturates was due not only to a growing awareness of the risks associated with their use, but also to the availability of safer, alternative hypnotics. A significant reduction in the proportion of overdoses involving non-barbiturate hypnotics is perhaps therefore unexpected. However, the majority of non-barbiturate hypnotic drugs are benzodiazepines, and the increased use in percentage terms in overdoses of minor tranquillisers, also mostly benzodiazepines, compensates to some extent for the reduced misuse of the hypnotic drugs.

It is of some interest to compare the findings in London A & E departments with those in other geographical areas. In Manchester, for example, a one-year study (1976–77) of deliberate self-poisoning revealed that barbiturates were taken in 11% of instances, and benzodiazepines in 39% (Sivner & Goldberg, 1978). In Belfast, a four-year survey (1973–76) showed that the commonest drug taken in overdose was a non-barbiturate hypnotic or tranquilliser, the main kind again being benzodiazepines (Hadden, 1978).

In 1982, in the USA, there were more than 120,000 emergency room drug abuse episodes reported through the DAWN system. Although alcohol in combination with another drug(s) was the top-ranked drug category, being used in 24% of all episodes, diazepam received the second largest number of mentions and was taken in 11% of episodes. Interestingly, in view of the increased proportion of overdoses in the UK involving minor tranquillisers, in some areas of the USA the number of mentions of diazepam decreased over the three-year period 1979–1981. The use of barbiturate hypnotics, not a major problem in the USA, decreased further, Tuinal (secobarbitone and amylobarbitone) being used in 2.2% of incidents in 1979, 1.9% in 1980, and failing to reach the "Top 20" in terms of mentions in 1981. Another point of interest from the DAWN survey of 1981 is that the average number of drugs mentioned in each episode was 1.6, the identical figure of both the 1975 and 1982 London surveys (NIDA, 1983). Comparison of different surveys in terms of demographic data is difficult, partly because of differences in tabulating results and also because of differences in methodology. In Manchester, the study included only those involved in episodes of deliberate self-poisoning, whereas the DAWN survey, like the London Casualty Survey, covered all those attending with a drug-related problem, (although DAWN only excluded children under the age of six).

In summary, the 1982 survey in London showed that there has been a slight reduction in the numbers of drug-related problems seen in A & E departments since 1975. This appears to be due to a reduction in the use of hypnotic drugs, including a striking reduction in barbiturate misuse, apparently related to their reduced availability.

The lesson for doctors, of the value of careful, responsible and frugal prescribing of all drugs that may become drugs of misuse is obvious. Apart from demonstrating recent trends in drug misuse, this study has confirmed in a broader sense the value of studies in A & E departments. A commitment by their staffs to complete the questionnaires ensures that information which would be gathered anyway is recorded in a uniform manner, while the usefulness and value of this information increases as more hospitals participate. The report of the Advisory Council on the Misuse of Drugs recommends that all Regions should monitor the extent and nature of drug misuse problems (ACMD 1982). It would seem that the A & E departments of hospitals in each Region offer an excellent opportunity to start this procedure with a minimum of delay and expenditure. Although these departments only provide information about one area of drug abuse, this is an area which is unrestricted by conventional preoccupation with dependence on one particular drug or group of drugs and which can make a valuable contribution to the total picture of drug misuse practices, and problems (Ghodse 1977).

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*Hamid Ghodse, MD, PhD, FRCPsych, *Consultant Psychiatrist, St George's, St Thomas' & Tooting Bec Hospitals*

John Stapleton, *Medical Statistician, Institute of Psychiatry, Denmark Hill, London SE5 8AF.*

Griffith Edwards, DM, FRCP, FRCPsych, *Director, Addiction Research Unit, Institute of Psychiatry.*

Thomas Bewley, MD, FRCP, FRCPsych, *Consultant Psychiatrist, St Thomas' and Tooting Bec Hospitals, London.*

Muhammad Al-Samarrai, MRCPsych, *Research Assistant, St George's Hospital.*

*Correspondence address: Drug Dependence Treatment and Alcohol Research Unit, St George's Hospital, Blackshaw Road, London SW17.

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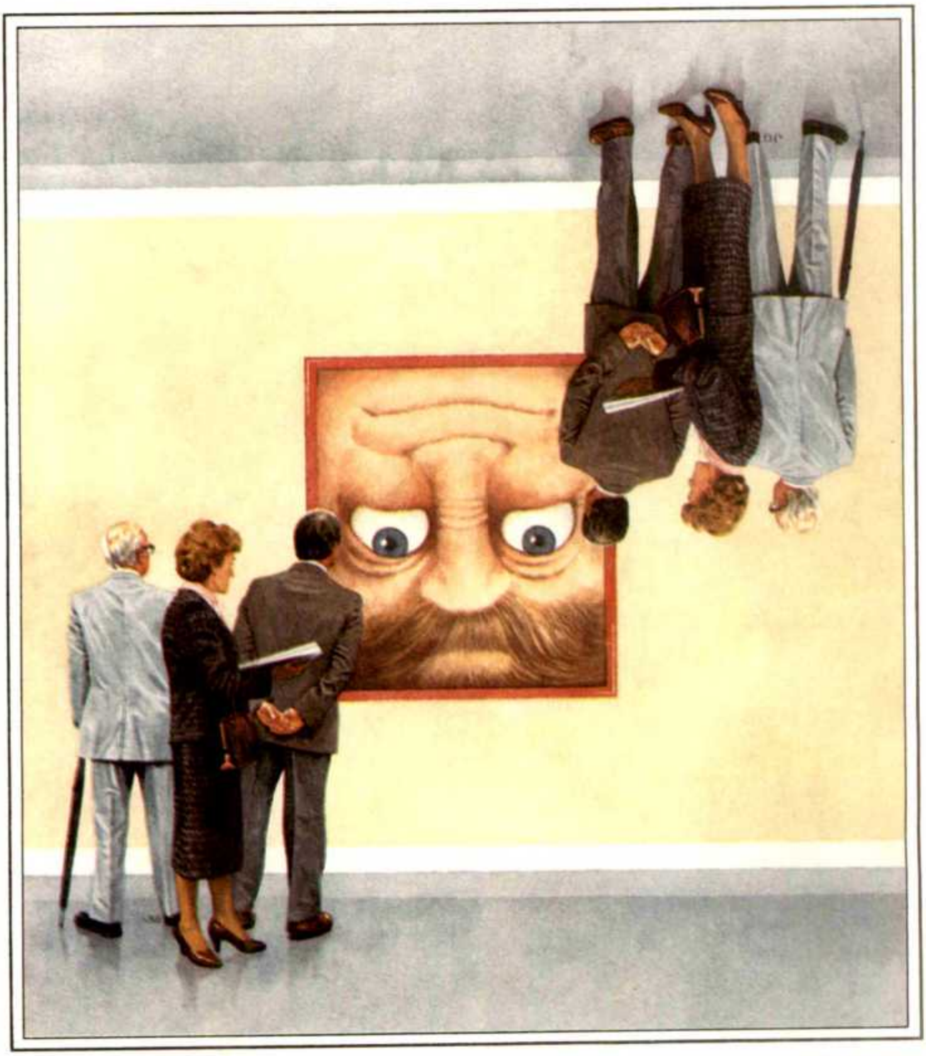

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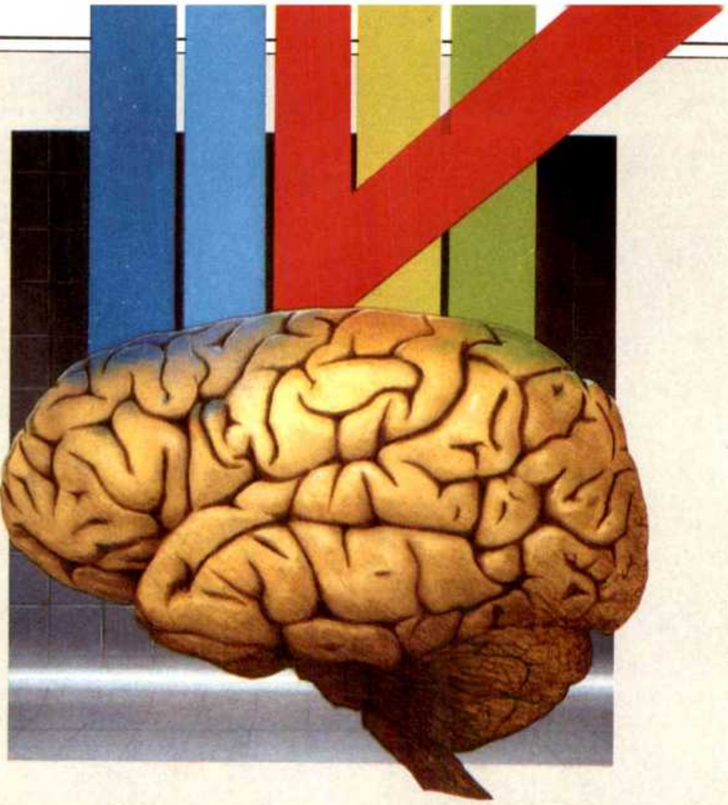

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What Happens when Psychiatric Out-Patients are seen Once Only?

LINDA GASK

The outcome of 30 new psychiatric outpatient consultations at which the psychiatrist decided to see the patient once only was examined after 3 months. Patients were referred from general practice, and evaluation was primarily from the viewpoint of practitioners; the majority were satisfied with a single consultation. However, only about half the patients were seen again by their GPs within the 3-month period, and most of the treatments recommended by the psychiatrists were not carried out by the GPs. Suggestions are offered to ameliorate this disturbing state of affairs.

Operational studies of outpatient clinics have revealed that between 14 and 23% (Johnson, 1973a, b) of new psychiatric patients are seen only once and then discharged back to their general practitioners (GPs). The effectiveness of these single consultations has never been examined. There is scanty evidence as to whether GPs would prefer more, or fewer patients to be immediately returned to their care.

Kaeser & Cooper (1971) in a study of referrals to the Maudsley Hospital outpatient and emergency clinics found that in only 16.4% of cases did the GP expect, or want to have continuing responsibility for the patients, and to be given advice on how to manage them. In only one-third of cases where the GP expected this outcome was his patient in fact referred immediately back to him. Johnson (1973b), however, looked at new referrals to clinics in Manchester, and found that in 49% of cases, the GP would have been happy to have been given advice only; despite this, a mere 23% were returned to his care. Johnson also demonstrated (1973a) that few of the patients followed-up as hospital outpatients had been offered any treatment that was not available in general practice.

If large numbers of patients are followed-up in the outpatient clinic for long periods, its functioning may become less than satisfactory. The purpose of continued attendance may be unclear, but unquestioned, by doctor and patient alike.

Blacker (1948) commented that when no clear decision was reached about the disposal of new patients, they could easily become regular attenders, briefly seen on each occasion for a check on their condition and a repeat prescription. Humphrey (1968) similarly wrote: "The psychiatrist provides first aid, the patient wonders vaguely whether this is all that specialist medicine has to offer and the GP is commonly none the wiser about his role." As more than three-quarters of psychiatric outpatient attendances are for follow-up (Department of Health and Social Security, 1984), it is important to consider whether they are really necessary.

Kessel (1963) suggested that some of these difficulties could be overcome by the greater use of the single consultation at the outpatient clinic. The psychiatrist could then, in uncomplicated cases, draw up plans—pharmacological or psychotherapeutic—which would be clear and simple enough for the GP to carry out; a realistic goal to aim for and a statement of prognosis would also be given. This would ensure the best possible use of psychiatric resources.

The present study examined the outcome of 30 new consultations with patients referred from general practice whom the psychiatrist had decided to see only once. Its object was to assess the effectiveness of a single consultation: evaluation was primarily from the viewpoint of the GP, who had continuing clinical responsibility.

Method

Patients selected were all referred by nearby GPs to general psychiatrists at the University Hospital of South Manchester. The psychiatrists, not the patient, had decided upon one consultation only, but eight cases were included where there was subsequent referral by the psychiatrist to a clinical psychologist or a psychiatric social worker, with the GP retaining clinical responsibility.

Over a four-month period between October 1982 and January 1983, 268 new referrals were seen by six consultants and six senior registrars; 45 of these were referred back to their GPs (16.8%). Of the 35 patients who met the above criteria, five were excluded because their GPs refused to be interviewed. This left a total of 30 patients of whom six were referred to psychologists and two to a psychiatric social worker.

The patients were referred by 26 GPs, all of whom were interviewed approximately 3 months after their patients had attended the clinic. The interviews were unstructured, but a particular effort was made to obtain answers to certain questions. These included the reasons for referring each patient, the GP's expectation of referral, his satisfaction with the outcome, whether or not he had carried out the advice suggested by the psychiatrist, and how well he knew the psychiatrist concerned. The GPs were also asked for their views on the psychiatric service provided by the department and, more specifically, on single-consultation referrals. The psychiatrists were asked what they expected to have happened to the patient after 3 months, and also for their views on single-consultation referrals.

Results

Patients

From a total of 30 cases, 14 patients were male and 16 were female, with a mean age of 41 (range 17–69 years). Their diagnoses, which were arrived at from perusal of the case notes and psychiatrists' letters, were: depressive illness, six; alcohol dependence, four; bulimia nervosa, two; grief reaction, one; phobic anxiety state, two; globus hystericus, one; organic neurasthenia, one; personality disorder, seven; no psychiatric disorder, six. None had a psychotic illness.

Interview with the GP

More than two-thirds of the patients were relatively well known to their GPs, and one-third had had previous contact with psychiatrists; one-third had been referred on first presentation of the problem to the GP. Factors leading to referral are summarised in Table I.

TABLE I
Factors leading to referral (more than one was occasionally given; n=30)

	Number of times noted	
Request of family or relatives	9	14
Request of patient	5	
Need for clarification of problem and/or confirmation of GP's own viewpoint	5	
Failure of treatment	6	
Treatment required not available in general practice	2	
Suicide risk	4	
Advised by hospital duty psychiatrist (after emergency assessment)	1	
Advised by surgeon	1	
Not known	1	

Half of the referrals had been suggested by the patients themselves or their relatives, which suggested that they did not perceive that their GPs were as competent to manage their problems as effectively as a specialist would. Six patients had been started on new medication so recently that the efficacy of this could not have been assessed before the decision to refer was made.

The GPs were asked how well they knew the psychiatrists concerned, e.g. by recognition from lectures, from medical student days, from telephone conversations, or personal contact; 17 of the 26 GPs knew the psychiatrists who had seen their patients.

The GPs expectations of the outcome of the consultations are shown in Table II. One-third expected a single consultation only, but half expected more from the hospital. As to what transpired, for 22 of the 30 patients, the GPs were happy with the single consultations.

Only 16 of the 30 patients had been seen at all by their GPs during the 3 months following referral. Of these, seven were thought to have improved, eight were unchanged, and one had deteriorated. The GPs could only state a view of their patients' opinions of the outcome of the referral in nine instances out of which six opinions were positive and three negative.

The psychiatrists had recommended treatment in 19 cases, and the extent to which their advice was carried out is shown in Table III. In 11 of the 19, the GP did not carry it out at all. In six of these, this appeared to have come about because the patient had not returned to see the GP; yet two of the six had affective disorders for which antidepressant medication had been advised, and two were dependent on alcohol.

Two-thirds of the GPs thought that referral had not resulted in their discovering anything they did not know already. This seemed to be because either they had expected more than they received from the hospital, or the psychiatrist's letter had not really answered the questions they wanted answering. Several GPs, however, felt more confident than before, and satisfied that they were not missing anything crucially important.

TABLE II
General practitioners' expectations of referral (n=26, GPs n=30 patients)

	Number of times noted
Out-patient care	7
Admission to hospital	1
Referral back to GP for continuing care	10
Specific form of treatment, e.g. psychologist, insight-orientated psychotherapy, day hospital (not included in out patient care)	7
None	5

TABLE III

Completion of psychiatrists' recommendations to GPs (further treatment by GP was recommended for 19 patients)

	Number of patients
Advice wholly carried out by GP	4
Advice partly carried out by GP	4
Advice not carried out by GP	11
Because	
GP agreed with advice but had delayed carrying it out	2
Patient had not been seen again	6
GP was seeking re-referral	1
Patient would not accept advice	1
GP totally disagreed with suggestion·	1

Most of the GPs thought that the psychiatric service provided by the department was good for the care of psychotic patients, but that the referral of neurotic patients was less helpful, both to themselves and the patients. Their expectation of benefit from referral for neurotic patients was low. When they were asked to compare their expectations of referrals to psychiatrists and of other hospital specialists, it appeared that less was expected of a psychiatric referral.

Sixteen of the 26 GPs interviewed thought that single consultations were useful, seven disliked them, and three had no view. Three wanted the patient to be seen again by the psychiatrist if the latter had recommended a change in treatment, and four clearly referred patients with the expectation of their continuing outpatient attendance. Those who found single consultations useful said they would be happy to supervise medication recommended by the psychiatrist, and one GP 'took it for granted' that psychiatrists knew he would be happy to have patients referred back to him.

Correspondence

In 25 of the cases, the GPs expressed clearly at interview what they had expected, yet only five of the referral letters contained a request for a specific treatment. The majority asked for 'opinion and advice'. In their responding letters, the psychiatrists mentioned diagnosis and treatment in 27 and 29 letters respectively, yet only four psychiatrists gave any indication of prognosis, and when to re-refer was only mentioned by 11. They noted that some nine patients had improved by the time they were seen in the clinic. This improvement was not related to the time between referral and appointment, but in five of the patients, it could have been related to the starting of new medication just before referral.

Interview with the psychiatrists

The psychiatrists were asked what they expected to have happened to the patients after 3 months. When, in the 19 cases where this was known, a comparison was made with the actual outcome, seven psychiatrists were approximately correct in their prognosis, seven were unduly optimistic, and five were unduly pessimistic. Only two psychiatrists frequently saw patients once only—one because of his belief that GPs should be able to carry out further care, given proper directions, and the other because of his high referral rate and good relationship with local GPs, who valued his opinion. Other psychiatrists, who less frequently saw patients once only, said they would assess whether they felt personally able to help, and would take into consideration the patient's relationship with his GP in deciding whether or not further care was best carried out by the latter.

Referrals to other professionals

Only one of the six patients referred by the psychiatrists to a psychologist had seen his GP within the 3 months. After that time, none of the six was still seeing a psychologist but, despite the GPs' continuing clinical responsibility, only two letters had been sent to them giving the psychologists' opinions or the outcome. Similarly, only one of two patients referred to a psychiatric social worker had seen the GP again, and in neither case had the psychiatric social worker told the GP or the psychiatrist what had happened to the patient.

Other findings

Analysis of the eight referrals where the GPs were dissatisfied with a single consultation revealed that in seven of these, the GP did not know the psychiatrist concerned, and in three cases a request for a specific form of treatment had been rejected by an unknown psychiatrist. Sixteen of the 22 GPs who were happy with the outcome knew the psychiatrist concerned, and these factors were found to be significantly associated (Fisher's Exact Test—$P = 0.005$).

Discussion

Despite the finding that the majority of the GPs interviewed thought single consultations could be useful, they were little used by the psychiatrists. Perhaps the concern expressed by many psychiatrists about the management of psychiatric illness in general practice influenced those in the present study in deciding to see most of their new patients more than once. Another possibility, however, is that the psychiatrists simply did not know that the GPs would have approved of single consultations.

The patients themselves were not interviewed in this study, so that it was impossible to discover accurately what they thought of the outcome of referral, or whether they thought that the consultations had been useful. The GPs were asked about their patients' views, but were able to report them in fewer than a third of cases. It also seemed that the GPs' replies were coloured by their own perceptions of the outcome.

The quality of communication between GPs and psychiatrists remained far from satisfactory. GPs' letters rarely mentioned a specific request, and frequently asked for 'opinion and advice'; at interview it became clear that this meant different things to different GPs. Since it does not convey what is really wanted, it would be better to give up this commonly used, but misleading phrase. GPs should state in their referral whether they are prepared to continue with the patient's treatment and management. The psychiatrists' letters were mostly unsatisfactory also, in as much as they failed to convey all the information that the GP would have needed in order to continue to manage the patient. Communication with the GPs was particularly poor when patients were further referred to psychologists or social workers. When such referral occurs, it should be clarified who retains clinical responsibility, and if this is the GP, he should be told what is happening. Kessel (1984) advocated greater use of the telephone in doctor-to-doctor communication. This is particularly necessary if the psychiatrist is going to adopt a different course from that which the GP puts forward in his referral letter. In such a case, there clearly needs to be discussion.

The problem of what happens to those patients who are not seen again by their GPs after they have seen a psychiatrist must be considered, if single consultations are to be more effectively used. The GPs studied had not seen half of their patients again within 3 months of the outpatient consultations. Patients do not always return spontaneously, and they need to be reminded to do so by both GPs and psychiatrists: GPs do not feel obliged to see a patient again after an outpatient consultation. In half the cases where treatment recommended had not been carried out, the reason was that the patient had not been seen again: this is disturbing. Some patients may have had acute problems, which rapidly resolved, but this is unlikely to be the explanation for the majority of such cases. If the GP waits passively for the patient to return, then the treatment recommended by the specialist will go by default. Such a passive approach is ill-suited to the known characteristics of psychiatric illness, since a failure to see the need for help may be part of the condition; indeed Forsyth & Logan (1968) pointed out that a system of outpatient care that puts too much dependence on the initiative of the patient will run into problems. The GP should insist on seeing a patient again after the specialist's letter has arrived..

The finding that single consultations were acceptable to the majority of GPs in this study suggests that they could be more widely used by psychiatrists.

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Linda Gask, MSc, MRCPsych, *Research Fellow, Department of Psychiatry, University Hospital of South Manchester, West Didsbury, Manchester M20 8LR.*

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Electroconvulsive Therapy as a Contributor to the Production of Delusional Misidentification

GEORGE G. HAY

Evidence for an organic component in patients with delusional misidentification syndromes is reviewed and three described who developed the Capgras symptom after a course of ECT which produced a mild organic psychosyndrome. The delusion was a complicating factor during treatment, but remitted in all cases as the organic brain syndrome cleared and the underlying condition improved.

The original description of the symptom by Capgras & Reboul-Lachaud (1923) referred to a female patient with a diagnosis of a chronic paranoid psychosis. For some time afterwards, it was considered a colourful delusion which could occasionally be seen in the setting of the schizophrenic syndrome. Later (Stern & MacNaughton, 1945), the symptom of delusional misidentification was reported in the setting of a primary affective illness—albeit a paranoid depressive psychosis with a marked colouring of suspiciousness. Eventually, cases of organic psychosyndromes were described (Weston & Whitlock, 1971; MacCallum, 1973; Christodoulou, 1977) in which the Capgras and similar symptoms were seen. It therefore became apparent that delusional misidentification, like all symptoms in psychiatry with the possible exception of the passivity phenomenon in schizophrenia, was non-specific, and could occur in a variety of psychiatric syndromes. The symptom itself has no diagnostic import.

However, a recent development—concurrent with the availability of more sophisticated investigative tools—has been the appreciation of 'organicity' in a significant proportion of patients with a basic diagnosis of a functional psychosis (Merrin & Silberfarb, 1976; Christodoulou, 1981). In other words, although paranoid schizophrenia seems to be the most common nosological setting in which delusional misidentification occurs, when these patients are investigated with sleep EEGs, brain scans, and formal psychometric testing, a strong organic component is found to be present in many of them, and to be contributing to the pathogenesis of the syndrome.

An analogy can be made with another rare condition—the Ganser syndrome. Originally described (Ganser, 1898) as an hysterical dissociative phenomenon, it was soon reported as a symptom that could be seen in the course of chronic psychotic illness (Nissl, 1902). This was followed by descriptions of typical Ganser states occurring in the setting of organic brain syndromes (Whitlock, 1967). Re-examination of Ganser's original publication in fact confirms that all three of his patients had a definite organic component to their illness: one had suffered from typhus and the other two had both sustained head injuries, with resulting loss of consciousness.

Hay *et al* (1974) described a patient who developed a Capgras symptom during the course of ECT prescribed for depression: this symptom was looked on as an epi-phenomenon, produced by ECT. When the delusion was present, there was a typical disturbance of the EEG, due to the electroplexy, whereas with remission of the symptom, the EEG returned to a normal pattern. Since that time, three further patients have been seen who have developed delusional misidentification only after the administration of ECT, given either for depressive illness or for schizophrenia with a marked affective component.

Case Histories

1. Miss L W, a 26 year-old single girl, was admitted urgently, giving a ten-day history of picking up "interference" from her television set, and feeling that people looked at her in an unusual way. She had been mute for long periods and was not eating properly.

She had a long previous psychiatric history, dating from the age of 19, when she had been admitted to a local hospital with what was diagnosed as a depressive stupor. Since that time, she had had two further episodes of in patient treatment—one for depression and one for a manic-like phase. She was being maintained on lithium carbonate. The family history was not contributory, and there was no previous medical history of note. She worked as a secretary, and lived at home with her parents.

On examination, she was perplexed, suspicious, and hesitant in manner; she was noted to stand still in the same place for long periods. She was almost mute, but with patience and coaxing, would answer some questions in a whisper: she described auditory hallucinations and said she thought she was God. She exhibited formal thought disorder and passivity ("a feeling of being controlled like a robot"). She said she felt extremely depressed, and a management problem developed because of her refusal to eat or drink. She was correctly orientated in time and place and denied drug or alcohol abuse.

A diagnosis of schizophrenic illness with a marked affective component was made, and it was decided to treat her with a course of ECT. After five treatments, she became labile in mood, aggressive in manner, and suddenly said that everyone had been "copied"—by which she meant that several of the other patients and nurses, and her visitors had been substituted by impostors who looked like them and pretended to be them. At the time, she was mildly clouded, and occasionally disorientated in time. As she was still not drinking adequate fluid the ECT was continued to eight treatments. She made a steady improvement: the delusional misidentification symptoms were fleeting, and remitted within ten days of stopping the ECT. She was discharged much improved, and has since been maintained on depot medication.

2. Mrs P K, a married women of 64, complained of feeling restless and withdrawn for three weeks; this dated from an unfortunate episode, when her uncle had collapsed and died whilst visiting her home. She had subsequently blamed herself for not reminding him to take his medication. There was nothing of note in her previous medical history, but she had had a depressive illness in 1981, treated with antidepressants to good effect. Her premorbid personality was that of a pleasant, sociable, and lively lady, interested in dancing and Yoga, and her family history was negative for psychiatric illness. She had been happily married for 40 years, and had one married daughter.

On examination, she was extremely tense, bemused, and puzzled. She was depressed and retarded, saying that she should not be in the hospital but a prison, that she was wicked, and had committed a crime. On occasions, she said that the police would be coming to arrest her, and she tried to leave the ward to report at a police station. She was correctly orientated in time and place, and her memory and cognitive functions were normal. A diagnosis of a depressive psychosis was made, and it was decided to treat her with a course of ECT.

After the second treatment she was less retarded, and said that the doctors caring for her were not in fact the same people who had admitted her, but had been substituted by plain clothes policemen who looked just like them. She therefore refused to talk to them, though she would still communicate with the nurses. On direct questioning, she stated that on one occasion, she had felt suspicious regarding her husband when he was visiting 'because his shoes just didn't look right', but the idea was not held with complete conviction. On reassessing her mental state, she appeared mildly confused and disorientated, with evidence of short-term memory defect. This dysmnesic syndrome was thought to be due to ECT, and the treatments were therefore given weekly rather than twice-weekly.

After the fourth treatment, she improved markedly and the idea regarding her doctors and husband disappeared; after six, she had made a complete recovery with no residual symptoms. She was discharged well, taking amitriptyline, 100 mg at night.

3. Mrs P L, a women of 30 with a history of recurrent episodes of schizo-affective illness, was admitted urgently in a state of distress and irritability, having received a demand for an unpaid television licence and a bill for repairs, which she had refused to pay. She was generally threatening in manner and uncooperative at interview. She appeared sad and tearful when talking of her problems and life circumstances, which she related with an air of suspiciousness. She stated that she thought she might have been adopted (there were no grounds for her saying this), and that she thought she was being watched and followed by the Social Services Department. When admitted, she still claimed that the Social Services Department were checking on her activities, and she demanded to take her own discharge for this reason, so that she had to be placed on a compulsory observation order.

There was nothing contributory in her previous medical history, but she had had recurrent episodes of psychotic illness since 1977, treated with combinations of neuroleptic drugs and occasionally ECT. It was decided to treat her with ECT and haloperidol. She had two treatments, then became much more hostile, and there was a disturbance when her husband visited: she said that he was not her husband at all but an impostor, who was either a psychiatric social worker or a community nurse. She said the Social Services Department had found someone who looked just like her husband, but in fact he was still at home, and the point of 'double' visiting was again to check on her behaviour; she told him to leave the ward and would have nothing further to do with him. At this time, she appeared bewildered and bemused, but formal cognitive testing was normal.

She refused to have further ECT, and treatment was continued with haloperidol with the addition later of lithium carbonate. After a week, her feelings regarding her husband abated, and she then allowed him to visit, saying she must have been mistaken in her accusations. Indeed, she made a steady and uncomplicated recovery, and was discharged symptom-free after a further three weeks. She has remained well since that time, apart from one episode of uncomplicated depression, and has remained on prophylactic lithium.

Discussion

In these patients, the primary or basic diagnosis was that of a functional psychosis of the type previously described as being prone to develop Capgras-like symptoms, in that the paranoid element was marked (Enoch & Trethowan, 1979; Todd *et al*, 1981). However, the actual Capgras symptom only developed during the course of ECT, and it can be hypothesised that the mild organic psychosyndrome produced by this treatment was sufficient to act as the precipitating or triggering factor for the development of the symptom.

It has been argued that as the Capgras symptom and prosopagnosia are characterised by disturbed ability for recognition and identification (Hayman & Abrams, 1977), "Prosopagnosia may be the primary expression of a specific cerebral dysfunction which forms the basis for a delusional elaboration resulting in the Capgras Syndrome". Cummings (1985) quotes delusional misidentification as being commoner in disturbances of the right (non-dominant) cerebral hemisphere. However, none of the present three patients were prescribed unilateral ECT to the non-dominant hemisphere, and all the treatments given were bilateral.

It would seem that there is now sufficient evidence in the literature of an organic component in the delusional misidentification syndrome to advise careful investigation of any patient for "organicity", even when a confident diagnosis of a functional psychosis has been made. In some cases, the treatment given for the primary condition, either neuroleptic drugs or ECT, may be the factor responsible for the development of this intriguing, rare, but fascinating symptom.

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George G. Hay, MD, FRCPsych, DCH, *Consultant Psychiatrist, University Hospital of South Manchester, West Didsbury, Manchester M20 8LR.*

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The Nottingham Experiential Day in Psychotherapy:
A New Approach to Teaching Psychotherapy to Medical Students

MARK AVELINE and JANE PRICE

A prime objective in teaching psychotherapy to medical students is to convey a practical understanding of what happens and a sense of the pleasure and responsibility of working with another person to improve the quality of their relationships. In Nottingham an experiential day was developed during the psychiatry clerkship; the teaching is by doing rather than describing, while spontaneity and individual expression are encouraged; the experience is valued by most and forgotten by none; it would be improved by a second experiential day or by a weekly forum for discussion of the personal and patient-care issues raised.

The medical undergraduate curriculum tends to emphasise the technical aspects of medicine, but psychotherapy is one of the few disciplines taught that attends specifically to patterns of human relationship, reaction, and feeling. It has a major contribution to make in demonstrating the importance of the human dimension in both illness and health. The contribution may be made on medical and surgical wards or, more commonly and as in Nottingham, during the psychiatry clerkship. How that contribution is made depends on the special nature of the subject, the time available, and the objectives set by the teachers.

Recent studies of factors influencing the choice of psychiatry as a career by medical students highlight an anti-psychiatric bias among non-psychiatric members of the teaching staff, peers, and house staff, together with a perception that the subject lacks scientific rigour. These negative influences are offset by directly seeing psychiatrists at work, and by having personal responsibility for patients during the clinical clerkship (Eagle & Marcos, 1980; Nielsen & Eaton, 1981; Crowder & Hollender, 1981; Brook, 1983; Wilkinson, Greer & Toone, 1983). Psychotherapy may be deployed in both the elucidation and care of medical and surgical problems, but the recognition that it is an essential component in the training of psychiatrists, together with its usual placing within the psychiatry attachment mean that its successful teaching faces the same obstacles as psychiatry itself. The same solutions would be possible in psychotherapy, were it not for two features: the content of the work, its confidentiality, and the patient's sensitivity over the matters being disclosed, place a constraint on observational methods of teaching, while the time-scale for change—15 months—far exceeds the duration of the clerkship. Unless special arrangements can be made (*vide infra*), this precludes the student from taking responsibility for a patient in psychotherapy.

Communication skills can and should be taught (Sanson-Fisher & Maguire, 1980); once acquired, these persist (Poole & Sanson-Fisher, 1980). The American psychotherapist Bruch (1981) has drawn a parallel between the learning the patient has to do and that which the trainee psychotherapist has to do—both are engaged in an active process of reappraisal. The therapist comes "to some living awareness of the significance and dynamic meaning of the interchange with the patient". However, psychotherapy cannot be properly taught at secondhand; it requires a living experience to bring home to the student some of the subtleties, stresses, and pleasures of working in this way with another person. Given sufficient time and resources, the training model pioneered at University College Hospital, London, and now implemented in the Department of Psychosomatic Medicine at Heidelberg University is ideal (Sturgeon & Knauss, 1979; Garner, 1981). Students have the opportunity to take responsibility for a patient, and work with him for up to 18 months; the cases are selected by the Department of Psychiatry and supervised in groups of six. This supervised experience allows ample space to explore the distressing and tragic issues of living and dying, trying and failing, and sometimes succeeding, that are inherent in medical life. Given the six hours of curriculum time available in Nottingham, other innovative solutions were needed.

In this teaching, there are four objectives, each lending itself to different solutions (Aveline, 1984). The first is to acquaint the students with the nature and special perspective of psychotherapy. An appropriate way is some form of direct experience of the subject, either through supervised practice or through membership of a personal group, ideally over the entire duration of the undergraduate course. The second is to teach what psychotherapy is and what it can achieve, how change occurs, in what setting and over what length of time; here, case discussion and role-play are appropriate means. The third is to inculcate some knowledge of what problems to refer and when; this would be best achieved by a factual handout. Lastly, we need to facilitate basic skills of listening, 'being with', and counselling (Wolff, 1971); role-play and supervised practice are the obvious candidates for achieving this. The Nottingham Experiential Day goes some way towards meeting each of these objectives, but gives particular emphasis to the first and the last.

The Nottingham day—context and content

Until the Spring of 1981, medical students in Nottingham received four one-hour lectures on psychotherapy during the ten weeks of the psychiatry clerkship, in the penultimate year of training. In this classical format, information was undoubtedly acquired, but what was not conveyed was a practical understanding of exactly what happens in psychotherapy, or a sense of the pleasure and the responsibility that goes with working with another person, to help him improve the quality of his relationships.

The Psychotherapy Unit secured a whole day for psychotherapy, replacing the lecture slots. We now report our experience with 15 experiential days.

Our goals for the day are:

(i) To acquaint students with our way of working in a personal way, so that they see the things we attempt to do and feel them, rather than simply hear from us about them;

(ii) To show what psychotherapy has to offer as a discipline, by increasing self-awareness and increasing sensitivity to the emotions present in any doctor–patient relationship;

(iii) To encourage students to see the value of spontaneity as a vital part of our work.

However, we do not see it as a form of therapy for students, and have no intentions of leaving people more disabled after the day.

By the end of the day, we hope that each student has an idea about the way our Unit runs, how we assess people as suitable for psychotherapy, how we decide on a particular form of psychotherapy suitable for that patient, and how we begin, maintain, and end therapy. We aim to give them a taste of both individual and group settings, and to demonstrate in a practical way how the members of the Unit work together.

We also aim to demonstrate to each of them that they have abilities to work in a similar manner with patients, and to heighten their awareness of themselves as developing, unique people, within the common framework of being doctors-in-the-making. We seek to explore the dynamics of the group they already work in, as a practical demonstration of group dynamics. We aim to keep the group active and constructive throughout the day, moving from theme to theme within a definite timetable. We do not attempt to focus on any one individual for a prolonged period of time, although we do give a clear message to students that if any of them find our day disturbing, they can contact any member of the Unit afterwards to talk things through.

Four weeks before one of the team meets the students for an hour to prepare them and give factual information about psychotherapy and the day. Certain anxieties are allayed, though doubtless others are raised. Students are reminded that the day is a compulsory part of their training, and are asked to come in casual dress and with food to share for lunch. As part of our commitment to seeing things through, the requirement that each student should be present for the whole of the day is particularly stressed.

The content of each day is the product of the interests and concerns of that particular group of students on the one hand and the preferred way of working of the staff members on the other. The day is adapted as it happens, to the needs of the students as they declare them and as we perceive them. Our boundaries are a start at 9.30 am and a finish at 4.00 pm, reserving time for the students to review and evaluate the day.

Typically, the day begins with interview skills enhancement, followed by an examination by the group of some common experience of medical student life; the latter generates more personal or intragroup themes, which are explored in the afternoon. In short, the day follows the natural progression in psychotherapy: as the staff are seen to be caring and respectful, so trust is developed; the events of the morning make possible the work of the afternoon.

Interview skills enhancement and basic concepts ($1\frac{1}{2}$ hours)

Numerous approaches have been tried. Video of an assessment interview or of components of the 'conversational model' of psychotherapy (Hobson, 1985; Maguire *et al.* 1984) have been viewed and discussed. Students have been asked to role-play breaking the news of death or terminal illness to relatives, or exploring the fears of a woman waiting for an operation for breast cancer the next day; the role-play may be videoed to facilitate detailed discussion. Alternatively, counselling exercises from Eagen's. 'The Skilled Helper' (1982) have been used.

The students' attention has best been engaged when they role-play psychotherapy patient and therapist. A staff member chooses an incident from a current therapy, and coaches one student into the role of that patient and the other into being the therapist; the 'therapist' can ask for help from his peers if he gets stuck, or someone can substitute for him. Also, the action can be suspended to allow the 'patient' to give feedback of his feelings and reactions to the therapist.

Initially, the dynamics of the case are not made clear, as our intention is to provide an opportunity to practice listening carefully to another, being warm and empathic, and to discover that doctors are capable of at least unconsciously knowing what is going on in the relationship. This discovery enhances the students' self-esteem, and demystifies the subject. It is then possible to discuss the structure of therapy, the likely outcome, and through an examination of the fit or misfit between the feelings and reactions of patient and therapist, to introduce the concepts of conflict, transference, and countertransference.

For this purpose, we have found it best to divide the group of 15 to 20 students into sub-groups of five to seven. The work of the small groups is improved by having the student choose which staff members to work with and which colleagues to group with.

Common experience in medical life (1½ hours)

At this stage, we propose exercises that will draw the group together by sharing some common experience or task, but which also highlight how different people are in their aspirations and perceptions. Energy is mobilised by warm-up exercises, and then the focus is explored by exercises which tap the student's ability to think creatively and symbolically (Aveline, 1979; Brandes & Phillipes, 1979; Remocker & Storch, 1982).

A favourite exercise is the time warp. The members of the group picture themselves one year, five years, and ten years hence. Volunteer students demonstrate their perceived future through sculpting—relationships are portrayed by posture and distance. Often the goal was being a consultant, a literally exalted position, but debate would be provoked by others placing family or children to the fore. One female student reflected her delight in being useful and strong by accumulating such burdens of responsibility that she was forced to her knees at the ten-year mark; in vivid form, she was faced with vital decisions.

Graffiti sheets may be pinned up on the walls. At one end of the room, students can write up their expectations on day 1 of what medical school would be like, and at the other, their experience of how it has been. This leads on to dividing the students into two or three groups, each with a staff member as a resource person, with the task of devising in half an hour a dramatic representation of medical student life, which they then perform and discuss. Again, individual and collective experience is given conscious expression; the content of this expression is discussed in the section 'Being a Medical Student'.

A more task-orientated approach is to brain-storm emotional issues that the students have difficulty in coming to terms with. Debate produces a list of three items, which are then worked up into illustrative dramas in the afternoon. Issues from one workshop were: talking about dying, delivering an abnormal baby, feeling angry with and alienated from 'neurotics', feeling helpless in the face of enormous loss, being weak and powerless in the medical system but at the same time being expected to be in the front line, and having to get 'hard' and not liking it.

Personal, intra-group or task themes (1½ hours)

Depending on how the morning has gone and what mandate the group has given, more difficult areas can be explored in the afternoon; the least stressful approach is the task-orientated drama. Generally speaking, in order of increasing stressfulness, these are: Secret Fears, the Magic Shop, Portraits, Group-sculpting, Sociogram, and the Persuasion Game.

In Secret Fears, each member of the group (including the staff members) writes on a slip of paper a minor secret about themselves that they would be embarrassed to disclose. The papers are distributed at random. Sitting in a circle, each speaks of the secret fear as if it was his own; others may explore how the speaker feels about that fear. This is an exercise in empathy, not in detection!

In the Magic Shop, the customer may purchase some personal characteristic that he desires, by trading for it some characteristic that he already has. Much debate was sparked off by one female student who began by wanting to sell her ability to have children, but decided in the end that there was nothing on the shelves of sufficient value.

In Portraits each student has half an hour to depict in paint the image he presents to the world; later, each explains the picture to the group. A variant is to have the picture discussed in pairs and then in the large group. The individual and the group gain an insight into how a person sees himself; quite often, missing and valued aspects are pointed out by the group.

Group-sculpting is a flexible informative technique: students volunteer to sculpt the group as they see it. When one group insisted on sculpting themselves as an undivided mass, the staff drew on observations made during the day, and remodelled the sculpture to show a more separated group, with some connections stronger than others and some students holding more central positions.

In a Sociogram, patterns of relationship within the group are indicated by answers to questions such as with whom would you go up a mountain, with whom could you argue, and who could you rely on. Answers are signalled by putting a hand on the shoulder of the chosen person or persons. The chooser and the chosen can be asked about the basis of the choice and about how it feels to be chosen.

These are powerful exercises which often make visible what was known and unspoken. While at the time some peripherally-placed students have had their sense of alienation heightened, feedback some weeks after the day has indicated that the group has been more aware of their positions and has brought them in.

To be successful at the Persuasion Game requires a robust competitive nature. A circle of seated students are paired with a standing student behind each chair: one chair is empty, and the person standing behind it has to persuade someone seated to come and sit on his or her chair, while the standing person who might be left has to attempt to dissuade him. The seated person is not allowed to speak until he/she has made the decision to stay or go.

Strong emotions are quickly stirred—sublime happiness when you persuade someone to move, dark despair when the fourth person turns you down; personal styles, subgroups, and relationships are highlighted, and students have the opportunity to be merciful or punishing. This exercise requires sensitive handling, and it is often best for the staff to join in.

In the final half hour, there is an open discussion, when we aim to put in perspective the experiences of the day. We discuss how and in what settings the exercises are used, and answer factual questions about psychotherapy. Sometimes the students feel too close to the day to want to discuss the subject on a factual level; sometimes through knowing of the approach at first hand, their questions are more searching and well informed. We remind the students that they can contact us for individual discussion of issues.

Being a medical student

We have now had the experience of working with approximately 250 students. The groups have greatly varied in ethos and personality, but certain tensions in being a medical student have recurred.

Judging from the graffiti sheets, students come to medical school looking forward to being useful, being intellectually stimulated, and meeting a lot of people. Excitement and freedom—especially from home and parents—are the keynotes. After 3½ years, many feel that their individuality is not being encouraged and that they have to conform; they feel they have become boring. Consultants are stuck-up and money is a prime objective. Reflecting what we suspect is a peculiarity of Nottingham, a significant proportion have become fundamentalist Christians, with that becoming their first priority.

In one most graphic visualisation, students represented the medical course as a machine which wrenched their skulls open, scooped out their brains, and stuffed in standard issue ones. Representations of the ideal course have emphasised greater choice, time to progress at different rates, time to take breath during the clinical period, and a personal relationship with their teachers. Some had achieved this, but a disquietingly large proportion had not.

Despite our knowledge of teachers who embody an holistic approach to every patient, technology and hard facts seem to dominate the thinking of most students. Female students were more likely to voice and feel comfortable with the personal. Perhaps not surprisingly in view of their youth—the early 20s—they did not feel confident in handling emotional situations. Over 3½ years, some of their natural interest in people as people had been dissipated.

In the groups, being openly competitive was difficult, as this was seen as threatening to the cohesiveness of the group; yet many, if not most, of the students are intensely competitive and will belong to a profession which is, in itself, intensely competitive. Students were reluctant to open up divisions and areas of dissent, which is understandable, as they had to get on with their colleagues while the group was together; they have no choice in the composition of the groups to which they are randomly assigned every few months. Nevertheless, denial was a common way of dealing with conflict; though railled against by the students, conformity was very much part of their psychological make-up, and led them not to protest. Conversely, to declare that they had needs was problematic; they seemed to feel their own integrity as people was being threatened. Emotionally (and financially), most depended upon their parents, and seemed not to question this; perhaps it was another aspect of their conformism.

Evaluation

Three sources of evaluation have been tapped—immediate, end of clerkship, and informal over the following months: the first two are more comprehensive. While comment in open discussion is always solicited, systematic feedback is gathered by having the students complete an anonymous written assessment before they finish the day. At the end of the clerkship, all students complete a written evaluation, which mentions the psychotherapy day among other events.

The majority of the students find the day 'fun'; they enjoy the 'games' and feel loosened up by the activities, though a minority find the games absurd. However, they often do not see how the experiences they have had link with the intention of teaching them about psychotherapy: 'interesting, enjoyable, but not useful in furthering understanding (of psychotherapy)' was a typical comment. In contrast, a few recorded that it was the first time that they had talked in detail about the issues that face them as doctors; they learned that talking about problems helps to come to terms with them. Few felt engaged by watching a video; they were bored and alienated by what seemed unnecessary jargon. Role-plays, dramas, and group sculpts caught their interest; they valued the opportunity to see the same situation from different people's points of view.

The students' overall reaction to the day took one of three forms. Some felt the day had gone just far enough and were satisfied with what they had seen and felt, some that it had gone more than far enough and had obviously been given food for thought, and some would actually have liked to take their learning about psychotherapy a step further. The use of the term 'fun' parallels these reactions: for some, it appeared to reflect a true feeling of relaxation and enjoyment, for others it was a defensive focussing on one aspect of the day to avoid considering its more personal and difficult aspects, and for yet others, it was a background experience that enabled important issues to be dealt with. Both staff and students considered that the day could be improved by holding a companion day or half-day soon after.

The day has already passed into the folklore of the medical school. New students have their perceptions of the day shaped by the old; this cannot be wholly bad as very few boycott it. Graduates of the day remember the events, and indicate that the dynamics of their group have altered. Differences between students have been more openly acknowledged and worked with; closer links have been made with isolated students.

Discussion

The purpose of our experiential day is to give the students a memorable and enjoyable illustration of psychotherapy; we provide a reasonably safe space in which the students can attend to and explore aspects of their personal and collective experience. Our hope is that they will catch some of our excitement with this work, and our teaching is by doing rather than describing; in this, we are moderately successful. As the psychotherapy team contains different disciplines and personalities, there was often animated discussion on how far to take the experiential element of the training day; this kept a fine 'edge' on the day, whilst allowing the exercise of reasonable restraint. Such a mixture in the team enhanced and enriched the day, and modelled a lively working relationship within a multidisciplinary team for the students.

Medical student training encourages the acquisition of facts, with a tendency to boil down each subject to a simple set of statements—what the subject is, how it works, the indications and contra-indications for referrals. This is a legitimate need for practitioners, who will need to know in general about the resources they can tap for their patients; the required facts are embedded in the experiences of the day, for the student who can abstract them, but this is difficult for most. While staff can see the significance of what is happening, many of the students perceive the events as meaningless happenings, rather than as illustrations of a special area of discourse. They lack the frame which would enable them to understand what is going on. Better preparation is needed; two instead of one pre-workshop seminars is one answer, a fact-sheet for study before the day is another.

The timing of the day in the clerkship is important. Preferably, it should be at the beginning of the psychiatry attachment, so that the work may be consolidated on the wards. We feel that one day is the minimum for this kind of experience, a second half-day or full day the following week would be advantageous. Ideally, the personal and patient care issues raised by the day should be followed up in small weekly discussion groups, led by psychotherapy unit staff or general psychiatrists. Much of the success is attributable to the extensive experience the staff have of the techniques used and of working together; staff with different interests would need to evolve other formats.

We are aware that there is a narrow dividing line between what we are offering and therapy, but the students' fantasy is that they may be forced into the role of patients or labelled as having problems. This is neither our intention, nor our practice: students set their own limits for self-disclosure, and these limits are explicitly respected. Our assumption is that all people have choices to make in their lives and that studying the interactions between patients and doctors and within groups assists the development of professional competence. Our use of particular techniques with the students illustrates how we would use similar techniques in our clinical work.

Each group varies in its interest in matters psychological; within groups, there may be rivalries, or needs to defend certain self-images, which impede full use being made of the day. Giving the students the opportunity to choose their companions in the small groups and to determine the level at which their small group will operate facilitates the day. This has led us to experiment with having three separate tracts within the day, each led by a member of staff, which allows the students to be at their preferred level; however, it is much harder work for the staff, and precludes the students from seeing how we work as a team.

We are concerned that so many students have described their medical course as stultifying and that their interest in people as people has been dissipated. We hope that this finding will be taken note of by course planners.

The nature of psychotherapy is slow work over many months to effect useful change in self-image and patterns of interaction. It could be argued that a single intense day gives a false impression of the subject, and might even encourage instant answers to personal problems that psychotherapists so deprecate. For our part, we are satisfied if the day raises questions in a way that stimulates the medical students to search for answers, and if they are once more appraised of the fact that the personal and the technical are indivisible parts of medicine. With some—probably those who are already open to the subject—we are successful; we need to investigate our failure to reach others; though systematic follow-up enquiries need to be made, we are not aware that any student has been harmed by the day. We regret the lack of opportunities to follow up our activities, and would prefer to provide a weekly forum for discussion over the ten weeks of the clerkship and beyond, if possible. Meanwhile, the experiential day is an unusual solution to a common problem of limited curriculum time and insufficient teachers.

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Mark Aveline, FRCPsych, *Consultant Psychotherapist, Nottingham Psychotherapy Unit, St Ann's Hospital, Porchester Road, Nottingham NG3 6LF*

Jane Price, MRCPsych, *formerly Senior Registrar in Psychotherapy, now Consultant Psychotherapist, Fair Mile Hospital, Berkshire*

*Correspondence.

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Electrocardiogram Changes and Therapeutic Desipramine and 2-Hydroxy-Desipramine Concentrations in Elderly Depressives

S. P. KUTCHER, K. REID, J. D. DUBBIN and K. I. SHULMAN

ECG parameters in elderly depressed in-patients were assessed during routine despramine treatment. Significant changes (prolonged PR and PRS intervals and a decreased QTc interval) were found, related only to steady state concentrations of desipramine's major metabolite—2-hydroxy-desipramine. Potentially clinically significant changes developed in 40% of the patients. All serum drug concentrations were within therapeutic limits. Previous assurances about despiramines's cardiac safety in the elderly may need to be re-evaluated.

Tricyclic antidepressants are commonly used in the treatment of elderly depressives (Salzman, 1982). In addition to their demonstrated therapeutic effectiveness, they are implicated in a wide variety of adverse effects, often resulting from their anticholinergic profiles (Hollister, 1979), and have cardiovascular effects that may complicate their use (Cassem, 1982). Although generally well tolerated (Glassman & Bigger, 1981), some studies have shown that they may produce significant disturbances of cardiac rate, rhythm, and conduction, and possibly may even be associated with sudden death (Boston Collaborative Drug Surveillance Program, 1972; Fowler *et al*, 1976).

Desipramine hydrochloride is an antidepressant that may have clinical advantages over other antidepressants in the elderly (Salzman, 1979); its relatively low incidence of anticholinergic side-effects may offer potential advantages in this age-group, Despite this, its cardiovascular effects in routine therapeutic use have not been well studied in the elderly, and although the measurement of serum desipramine concentrations may have therapeutic utility (Nelson *et al*, 1982), there is insufficient appreciation of the relationship between cardiac abnormalities and either steady state concentrations of desipramine or its major metabolite 2-hydroxy-desipramine. Such knowledge is of clinical importance in the elderly, many of whom are at risk of developing a cardiac disorder.

Electrocardiogram (ECG) studies of young patients have documented increased PR and QRS intervals, along with changes in heart rate, QTc and T-wave amplitudes, associated with desipramine treatment (Veith *et al*, 1980 ; Rudorfer & Young, 1980). Attempts to correlate these changes with serum desipramine concentrations have yielded equivocal results; neither the studies by Veith (1980) nor by Rudorfer (1980) showed a strong relationship between ECG changes and desipramine serum concentrations. However, neither author measured 2-hydroxy-desipramine concentrations, although Veith noted that desipramine metabolites might be associated with some of the conduction changes described. The study by Cutler *et al*, (1984) of desipramine side-effects in four elderly depressed women, although measuring 2-hydroxy-desipramine levels, did not evaluate ECG changes.

We report here an open clinical study on the ECG changes with desipramine treatment in a population of elderly depressives. It is, to our knowledge , the first study to investigate the relationship between ECG abnormalities and steady state desipramine and 2-hydroxy-desipramine concentrations in elderly patients.

Method

The study population consisted of ten consecutively assessed elderly inpatients (mean age 70·8, range 60–85 years; seven female, three male) who met DSM III criteria for major depressive disorder and scored a minimum of 25 on the 17-item Hamilton Depression Rating Scale (Hamilton, 1960). No patient was suffering from an acute medical illness nor taking drugs that would have affected the ECG. All had normal liver, thyroid and hematological indices; one had a pre-existing cardiac condition—a stable sub-endocardial infarct. All scored 29 or above on the mini-mental status examination (Folstein *et al*, 1975). The reasons for the study were explained and understood by the patients, and ethical consent was obtained.

A pre-treatment ECG was taken, along with a full medical assessment. Each patient was treated independently with desipramine hydrochloride by one of three different

TABLE

ECG changes and desipramine and 2 hydroxy-desipramine serum concentrations in elderly depressives

ECG variable	*ECG change (seconds)*		*Desipramine*		*2-hydroxy-desipramine*	
PR	0.017 ± 0.004	($P=0.003$)**	$r=0.17$	($P<0.62$)	$r=0.86$	($P=0.002$)**
QRS	0.5 ± 0.16	($P=0.015$)**	$r=0.10$	($P<0.77$)	$r=0.08$	($P<0.82$)
QT	-0.01 ± 0.008	($P<0.09$)	$r=0.32$	($P<0.36$)	$t=0.52$	($P<0.14$)
QTc	-0.03 ± 0.017	($P=0.002$)**	$r=0.05$	($P<0.87$)	$r=0.66$	($P<0.04$)**
HR*	-3.1 ± 2.7	($P<0.28$)	$r=0.32$	($P<0.35$)	$r=0.25$	($P<0.51$)

*—Heart rate is in beats per minute

**—Significant

clinicians. Dosage was adjusted according to each clinician's judgment of the drug therapeutic effect. After the fourth treatment week, and at least ten days following the last adjustment of the desipramine dose, the ECG was repeated, and venous blood samples collected 10–14 hours after the last dose of desipramine, using venoject tubes.

The plasma was separated, and stored in glass tubes at −40°C until analyzed; initial samples were divided and 2·5 mls used to obtain desipramine concentrations, determined by capillary column gas chromatography using a DB-17-capillary column. 2-hydroxy-desipramine concentrations were analyzed by high-pressure liquid chromatography technique, using a CB 18 column, with 5·0 cc of blood from the same sample. A mobile phase carrier, consisting of 300 cc of HPLC grade methanol and 200 ml of acetate buffer (0·1 molar) ph 5·5, was used as the carrier for the analysis. Visual measurements were obtained using an electrochemical detector.

The ECGs were analyzed by a cardiologist, blind to the patient's condition and not involved in the patient's care. In addition to the 20 ECGs analyzed from the sample subjects, 20 additional ECGs were selected at random from the other patient's records, and included in the analysis, to ensure objectivity. The data were analyzed using the paired student's t-test and Spearman's rank correlation coefficient.

Results

The mean steady state desipramine concentration was 352±259 nmol/L, (range 113–895 nmol/L). Effective treatment steady state serum levels in the elderly are not precisely determined, and the guideline of 500 to 1000 nmol/L (125 to 300 ng/ml), as determined by our laboratory, was used; this was based on available literature, which suggests that desipramine concentrations are related to treatment response, as follows the recomendations of Nelson *et al*, (1982). None of the patients exhibited drug toxicity, either clinically or by steady state serum concentrations.

Treatment-related ECG changes

PR interval

Desipramine treatment was associated with a prolonged PR interval ($P=0{\cdot}003$) (Table); there was no correlation between PR interval and steady state desipramine concentrations, but a significant correlation between prolongation of the PR interval and steady state 2-hydroxy-desipramine concentrations ($r=0{\cdot}84$, $P=0{\cdot}002$).

QTc interval

The QTc interval was significantly decreased ($P=0{\cdot}002$), but there was no correlation between QTc interval and steady state desipramine concentrations (Table). There was, however, a significant correlation between QTc interval change and 2-hydroxy-desipramine concentrations ($r=0{\cdot}66$, $P<0{\cdot}04$).

QRS interval

The QRS Interval was prolonged ($P<0{\cdot}01$) with desipramine treatment, but this change was not correlated with either desipramine or 2-hydroxy-desipramine concentrations (Table).

QT interval

The QT Interval was not significantly changed by desipramine treatment, and was not related to any of the drug concentrations (Table).

Heart rate

Desipramine treatment did not significantly alter heart rate (Table).

Other changes

Four post-treatment ECGs showed rate or rhythm changes of potential clinical concern. One showed a sinus tachycardia, one poor R wave progression to V3, and two a first-degree atrioventricular block. There was no firm relationship between these changes and steady state desipramine or 2-hydroxy-desipramine concentrations, but in three of these patients the 2-hydroxy-desipramine levels were above the patient mean.

Discussion

The results of this study show that elderly depressives treated with therapeutic levels of desipramine hydrochloride do exhibit some significant changes in ECG parameters: the PR Interval and QRS complexes are prolonged, while the QTC is decreased. Unlike results of studies in younger patients (Veith *et al*, 1980; Rudorfer & Young, 1980), the heart rate and the QT Interval were not affected. Further, both the PR and QTc changes were significantly correlated to steady state 2-hydroxy-desipramine concentrations; there was no correlation of any ECG parameter to steady state desipramine concentrations. Other potentially significant ECG changes such as sinus tachycardia, poor R wave progression, and first-degree atrioventricular block, although not consistently related to any steady state drug level, tended to be found in those patients with 2-hydroxy-desipramine concentrations above the mean. Nevertheless, all serum measurements were within the therapeutic range.

Although tricyclic antidepressants when properly used, are effective and relatively safe (Glassman & Bigger, 1981), desipramine's potential cardiotoxicity in a population at risk has not been adequately evaluated. Available data concerning its anticholergic side-effects identify the elderly as a group at risk, but previous reports of its low cardiotoxicity have not considered its effect on the ECG (Cutler *et al,* 1984; Nelson *et al,* 1982). Cutler *et al,* for example, concluded that desipramine has a "lack of cardiovascular effects", and supported its use in elderly female depressives on the basis of a study of four desipramine-treated patients, in whom only heart rate and blood pressure were measured. Our study provides evidence to question these conclusions, documenting significant changes in PR, QRS, and QTc Intervals, and a 40% incidence of potentially problematic ECG changes occurring at steady state therapeutic serum concentrations of desipramine. Further, these effects seem to be related not to the concentrations of desipramine itself, but to those of its major metabolite 2-hydroxy-desipramine.

Although the pharmacology of desipramine is generally know, that of its hydroxylated metabolite 2-hydroxy-desipramine, is less well appreciated (Jefferson, 1975). Desipramine is cleared largely by hydroxylation and subsequent conjugation at the 2 position (De Vane *et al,* 1981); hydrodxylation efficiency varies greatly amongst individuals, and may be less efficient in the elderly (Bock *et al,* 1983). *In vitro,* both animal and clinical studies have demonstrated remarkably similar kinetics of both compounds (De Vane *et al,* 1981; Potter, *et al,* 1982; Javaid *et al,* 1979). 2-hydroxy-desipramine, like its parent compound, is a potent norepinephrine uptake inhibitor, with weak serotonergic and dopaminergic system effects (Potter *et al,* 1979; Javaid *et al,* 1979). However, its central effects may be greater than those of desipramine, since increased CSF ratios of 2-hydroxy-desipramine/desipramine over those found in plasma have been reported (Potter *et al,* 1982), though to date, this has not been therapeutically çonfirmed (Nelson *et al,* 1983).

Animal and *in vitro* studies of desipramine have shown it to exhibit a direct cardiac effect not dissimilar to that of quinidine, including impaired AV conduction, a prolonged PQ interval, and decreased V_{max} of the ventricular action potential (Bianchetti *et al,* 1977; Tamargo *et al,* 1979). However, 2-hydroxy-desipramine effects were not assessed in these studies. Studies of direct 2-hydroxy-desipramine cardiac effect are few, but report more cardiotoxicity for 2-hydroxy-desipramine than for its parent compound (Potter *et al,* 1983; Javdhyala *et al,* 1977). Further, the latter authors demonstrated a narrow range between doses of 2-hydroxy-desipramine that elicit minimal cardiac effects and those which significantly depress the myocardium. The reasons for this are unclear, but possibilities include an increased affinity of 2-hydroxy-desipramine for cardiac tissue, or less extensive binding to plasma constituents. It may be that the cardiotoxic effects of desipramine are in the main due to its hydroxylated metabolite.

Clinically, the cardiac effects of 2-hydroxy-desipramine may be more severe in the elderly, although the reasons for this are also unclear. Possible age-associated differences in free-bound ratios and metabolic degradation between desipramine and 2-hydroxy-desipramine cannot be ruled out in this population (Nies *et al,* 1977). The exception to this is in effect on heart rate, in which this study confirms the findings of Cutler *et al,* (1984) that contrary to results in younger populations, there was no significant increase in the heart rate of elderly depressives. This may be secondary to decreased β-receptor sensitivity found in the elderly (Vestall *et al,* 1979).

Although a one-to-one relationship between significant ECG changes and risk for cardiac complications during desipramine treatment has not been uneqivocally established by this study, our data suggest that earlier clinical certainty about the cardiovascular safety of elderly depressives treated by desipramine needs re-evaluation. Our finding of significant ECG changes at therapeutic desipramine concentrations suggests that elderly patients treated with desipramine should undergo regular ECG monitoring, and that changes in dosage should be evaluated by both clinical response and cardiovascular effects. Further, althought the caution expressed by Nelson *et al,* (1983) about the usefulness of routine monitoring of 2-hydroxy-desipramine concentration in patients has merit, elderly depressives may be a select population, in which appropriate serum monitoring of 2-hydroxy-desipramine levels is clinically useful.

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*S. P. Kutcher, BA, MA, MD, FRCP (C), Dip Child Psych, *McLaughlin Fellow, M.R.C. Brain Metabolism Unit, Royal Edinburgh Hospital, Edinburgh, Scotland EH19 5HF. Present Address: University of Toronto, Department of Psychiatry, Sunnybrook Medical Centre, 2075 Bayview Avenue, Toronto, Ontario, Canada.*

K. Reid. PhD, *Director of Laboratories, Queen Street Mental Health Centre, 1001 Queen St. W., Toronto, Ontario, Canada.*

J. D. Dubbin, MD, FRCP (C), FACC. *Staff Cardiologist, Sunnybrook Medical Centre,*

K. I. Shulman, MD. MRCPsych. FRCP (C), *Coordinator Division of Geriatric Psychiatry, Sunnybrook Medical Centre.*

*Correspondence

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Threatening Life Events in the Onset of Schizophrenia, Schizophreniform Psychosis and Hypomania

R. K. CHUNG, P. LANGELUDDECKE and C. TENNANT

In a study of cases of recent onset of schizophrenia, schizophreniform psychosis and hypomania (DSM-III criteria), threatening life events were significantly related to the onset of schizophreniform psychosis but not schizophrenia. The results also suggest that threatening events may precipitate hypomanic episodes.

Empirical studies first examined the relationship of life stress to the onset of psychiatric disorders in the latter part of the 1960s. Brown & Birley (1968) reported an excess of threatening life events in the three weeks prior to onset of acute episodes of schizophrenic illness. There have since been at least 15 studies in this area (see reviews by Dohrenwend & Egri, 1981; Day, 1981; and Rabkin, 1980), but the evidence that stressful events play a substantial role in the onset or relapse of schizophrenia or related disorders is still relatively weak.

Interpretation of earlier research findings has been hampered by a variety of methodological flaws. Firstly, life events were often assessed in the period prior to the date of hospital admission rather than the date of onset of disorder, so that the role of stressful events in the onset of disorder itself could not be ascertained. Secondly, events which were not independent of the effects of the illness were often included in analyses. Finally, in only three studies have 'normal' control subjects been used (Schwartz & Myers, 1977*a,b;* Jacobs & Myers, 1976; Brown & Birley, 1968), the remainder simply relying on comparisons with other groups of psychiatric patients. Thus it was not possible to draw from conclusions about events in relation to schizophrenic onset.

An assessment of the few studies with acceptable methodology still provides inconsistent evidence of a substantial role for life events in schizophrenia. Of the three studies involving normal control subjects, two show an association between independent stressful events and the onset of illness while the third (Jacobs & Myers, 1976) does not. A further important study is that of Leff *et al* (1973), which showed independent life events to be associated with relapse in schizophrenic patients on active medication but not in those on placebo. In a more recent study, Leff *et al* (1983) found that life events precipitated relapse only in patients from high 'expressed-emotion' families. Finally, in an interesting prospective study of US Army recruits, Steinberg & Durell (1968) found that the monthly rate of admission for schizophrenia in the first months of induction was six times the average monthly rate for the second year of military service.

Similar methodological problems have flawed the few studies on the relationship of life event stress to hypomania. Glassner & Haldipur (1983), who did not include a 'normal' control group, found that late-onset subjects who relapsed with bipolar disorder (depression or hypomania not specified) had associated precipitants. Ambelas (1979) assessed hypomanic patients in the period prior to admission (not onset), and found that they had experienced more events than surgical controls. However, in a similar study assessing life events prior to admission, Kennedy *et al* (1983) found no difference between hypomanics and controls. Finally, in an uncontrolled study using a crude life events inventory, Dunner *et al* (1979) found that 73% of male manic onsets and 31% of female manic onsets were associated with a significant event. For depressive onsets the reverse trend was observed, with 26% of males and 64% of females reporting a significant event.

In short, the empirical evidence that life events precipitate either acute schizophrenic episodes or hypomania remains sparse. Research in this area has recently been facilitated by developments (i.e. DSM-III) both in the assessment of life event stress and in the domain of formal diagnostic criteria for psychiatric disorders. However, a more sophisticated contextual threat approach to assessing the threat of life events has been developed by Brown & Harris (1978). This has the advantages of providing both a more sensitive and yet objective rating of threat or stress, and a judgement as to the independence of events from the disorder. Thus, if any association is found between the illness in question and the life events an appropriate causal relationship may be presumed. To date this approach has only been used in one study of schizophrenia (Leff *et al,* 1983). In terms of psychiatric classification, the introduction of DSM-III has led to the definition of a variety of disorders which were formerly subsumed under the broad diagnosis of schizophrenia (e.g. schizophrenia, schizophreniform psychosis, atypical psychoses, brief reactive psychosis. As yet, no study has reported an association between life events and these various disorders.

The present study, using the contextual threat assessment of life event stress and DSM-III diagnostic criteria, examined the relationship of threatening events to the onset of non-organic, non-depressive psychotic disorders: schizophrenia, schizophreniform psychosis and hypomania. Patients with these disorders were compared with healthy control subjects, matched for age and sex.

Method

Medical and nursing staff in four teaching hospitals, two regional psychiatric hospitals, and one private in-patient psychiatric hospital in Sydney were approached to obtain appropriate patients admitted over a four week period. For inclusion, patients had to be aged between 16 and 65 years and to have a DSM-III diagnosis of schizophrenia, hypomania, schizophreniform psychosis, atypical psychosis, or schizoaffective disorder. Patients were only included if the onset or relapse of their psychiatric disorder could be accurately dated to within 12 months of their present admission to hospital. In addition, subjects had to have been free from psychotic symptoms for the six months prior to the onset of their current acute illness—this being the period over which their pre-morbid life events were assessed. Patients with organic psychoses were excluded.

Control subjects derived from two sources. The first group ($n=12$) were subjects, matched for age (within five years) and sex, who were randomly selected from the state electoral roll. Because the process of obtaining these controls proved difficult, we included another group ($n=28$). These were surgical admissions, matched for age and sex, whose illness was of short duration and in whom positive pathology was identified (e.g. acute appendicitis proven by histopathology, perianal abscess, pilonidal sinus, anal fissure etc); patients with disorders that could have been caused by stress (e.g. trauma or duodenal ulcers) were excluded. All controls were briefly screened by means of an interview for presence of affective and schizophrenic disorders.

The dating of onset of the patient's illness was determined by a review of case notes together with interviews with the patients, therapists, and relatives if necessary. The following types of onset were recognised: from 'normal' to psychotic symptoms; from 'normal' to prodromal symptoms; and from residual to psychotic symptoms (DSM-III criteria). If the onset was insidious and could not be dated, or if the patient did not have a six-month period free of psychotic symptoms, then this subject was excluded.

The patients were interviewed while in hospital, after the acute symptoms had remitted; the diagnoses and the dates of onset were confirmed, and Brown & Harris' (1978) structured life events interview administered. The interview covered a six month period prior to the onset of the acute illness, both in the psychiatric patients and the surgical controls, and six months prior to interview for the controls from the electoral roll. Vignettes of each event and chronic difficulty were objectively rated for threat, using Brown & Harris' four-point scale; only events of ratings 1 and 2 were deemed 'threatening'. The rater was blind to the status of the subject at this stage. One 'threat' rating was obtained for chronic difficulties, and two for each life event: 'long-term threat' (threat at one week, as defined by Brown & Harris) and 'extra long-term threat' (threat at three months). The latter had not formerly been evaluated. The events were then assessed and evaluated as to whether they were independent of the effects of the illness. Ratings were: independent, probably independent, and dependent. The latter were excluded from analyses. Events were also coded by type: personal illness, other's illness, deaths, role changes, news/crises, employment, finances, housing, marital, and miscellaneous. Statistical analysis was by chi squared analyses of cross-tabulated data. For 2 × 2 tables, when there were fewer than 21 cases or expected cell frequencies were less than 5 in 20% of cells, Fisher's exact tests were performed. Yate's corrected chi squared test was applied for all other 2 × 2 tables. The critical level for statistical significance was set at 0.05.

Results

The sample

The case records of 96 patients were initially screened and discussed with their treating doctors; 55 subjects were excluded on the grounds either that their disorder was of more than 12 months' duration or that there had been no pre-morbid psychosis-free period of six months or more in the previous twelve months. Of the remaining eligible subjects ($n=41$), 40 agreed to be interviewed. Their diagnoses were schizophrenia (15), schizophreniform psychosis (9), hypomania (14), atypical psychosis (0), and schizoafffective disorder (2); the latter two diagnostic groups are not discussed further. The three types of onset have already been mentioned (normal to psychotic symptoms, normal to prodromal symptoms and residual symptoms to psychotic symptoms). The numbers of schizophrenics in these groups were 5, 0, and 10 respectively, and of schizophreniform disorders, 7, 2, and 0 respectively. The other diagnoses were all 'normal to psychotic' presentations.

The schizophreniform patients, with a mean age of 27.1 years, were significantly younger than both hypomanics (38.1 years, $t=2.3$, $P<0.05$)) and schizophrenics (40.0 years, $t=2.4$, $P<0.05$). The mean ages for the three control groups were 28.8, 37.4 and 40.1 years respectively. The sex distribution was not significantly different in the three groups of patients, the proportion of males being 56%, 43%, and 47% respectively. The three groups of patients

TABLE I
Marital status of patient and control group

Diagnosis		*Marital status (n)* *Married*	 *Single, divorced, widowed, or separated*
Schizophrenia	Patients	3	12
	Controls	10	5
Schizophreniform psychosis	Patients	1	8
	Controls	4	5
Hypomania	Patients	4	10
	Controls	11	3

TABLE II
Employment status (prior to admission) of patient and control group

Diagnosis		*Employment status (N)* *Employed*	 *Unemployed/ domestic duties*
Schizophrenia	Patient	1	14
	Control	10	5
Schizophreniform psychosis	Patient	3	6
	Control	8	1
Hypomania	Patients	7	7
	Control[1]	9	4

[1] Employment data was missing for one control subject.

were comparable in terms of marital status (Table I). However, two significant differences emerged between the patient and control groups: schizophrenic patients were less likely to be married than their age and sex-matched controls ($\chi^2=6.7$, df=1, $P<0.01$), as were hypomanics ($\chi^2=7.1$, df=1, $P<0.01$).

Of the 15 schizophrenic patients only one was in paid employment, the remainder being either unemployed ($n=11$) or performing domestic duties (Table II). A significantly greater proportion of the schizophrenic control subjects than patients were in paid employment ($\chi^2=11.6$, df=1, $P<0.01$). Similar findings emerged for the schizophreniform psychosis patients and controls, with only one third of the patients being in paid employment; one further subject performed domestic duties. A significantly greater proportion of control subjects were currently paid employees ($\chi^2=5.8$, df=1, $P<0.05$). Of the hypomanic patients, half ($n=7$) were in paid employment, a further 15% ($n=2$) did domestic duties, and the remainder were unemployed, The hypomanic controls were comparable as regards the proportion in paid employment. Comparison of the three groups of patients in terms of the proportion who were in paid employment revealed the difference to be significant ($\chi^2=6.7$, df=2, $P<0.05$).

Life stress

Chronic difficulties

The frequency of total chronic difficulties did not differ significantly in any of the three groups of patients, when compared with their controls. Similarly, a comparison of these groups failed to reveal any significant differences between them. Individual analyses of the frequency of chronic difficulties according to their threat ratings (i.e. 1,2,3 and 4 analysed separately) also revealed no significant differences either between different groups of patients or between the patients and their controls. The small sample size, together with the low frequency of chronic difficulties involving significant threat, may have been responsible for these findings.

Life events of significant long-term threat (ratings 1 and 2)

The occurrence of events of long-term threat over the 26 week period prior to onset of psychiatric symptoms is given in Table III. Significantly more schizophreniform patients than controls had experienced such events ($\chi^2=6.1$, df=2, ($P<0.05$); their rate was six times that of their controls. Similarly, a greater proportion of schizophreniform patients had experienced threatening events in

TABLE III

'Threatening' life events (ratings 1 and 2) in patients and controls

Diagnosis	*Patients*		*Controls*	
	Events	*No events*	*Events*	*No events*
Schizophrenia ($n=15$)	5	10	5	10
Hypomania ($n=14$)	2	12	1	13
Schizophreniform psychosis ($n=9$)	6	3	1	8

comparison with the hypomanics ($\chi^2=7.3$, df=2, $P<0.05$). Although the proportion of hypomanics experiencing such events was double that of their controls, the difference failed to reach statistcal significance. The proportions of schizophrenics who have experienced recent threatening events was comparable to that of their controls.

It is possible that demographic differences between the schizophreniform patients and the other groups might be responsible for observed differences in terms of frequency of threatening life events. Firstly, the schizophreniform patients tended to be younger than the other groups of patients; previous studies have suggested that younger subjects may experience more stressful events than older ones (Tennant, 1977). Secondly, the schizophreniform patients were more likely to be unemployed than their controls, and it is plausible that the occurrence of threatening events is more common in the unemployed. However, these factors are unlikely to be responsible for the greater frequency of threatening events in the schizophreniform patients, given that there was no significant association between the occurrence of threatening life events and the socio-demographic variables of age, sex, marital status, and occupational status.

The analyses for 'extra long-term threat ratings' (i.e. threat assessed three months after the event) revealed no significant differences between any of the three groups of patients or between the patients and their respective controls. Limited statistical power, due both to the infrequency of events with a threat rating of 1 or 2 three months after the event, and to the small sample size in the present study, may have been largely responsible for these negative findings.

An analysis was made of threatening events (long-term and extra long-term) occurring within the periods of 0–4 weeks, 0–13 weeks and 13–26 weeks before onset. No significant differences emerged between the groups of patients or between patients and controls, with one exception: for the period 13–26 weeks before onset, schizophreniform patients had more events of long-term threat than controls ($\chi^2=7.3$, df=2, $P<0.05$). Since Brown & Birley (1968) reported that life events precipitated acute schizophrenia in the three weeks prior to onset, we looked more closely at events in a comparable period (four weeks) before onset in the three groups of patients and in controls. The frequency of events of long-term threat (ratings of 1 or 2) in the patients and their controls were 27% and 7% respectively for schizophrenics, 22% and 11% respectively for hypomanics, and 7% and 0% respectively for schizophreniform psychotics. The differences between patients and controls failed to reach statistical significance. Again, the small sample size and the relatively low frequency of events assessed in these shorter periods may have contributed to these negative findings.

Events of minimal or no threat (ratings 3 or 4)

None of the 18 analyses of events of 'minimal' long-term threat (rating 3) showed a difference between groups of patients, or between patients and controls, over the 4 weeks, 13 weeks or 26 weeks prior to onset. The analyses of events of 'no' long-term threat (rating 4) were not significant, with the exception of hypomanics and their controls: hypomanics were significantly less likely to have non-threatening events in the 13 weeks (Fisher's exact $P=0.008$, c.f. $P=0.001$ for controls) and 26 weeks before onset than their controls.

Events by type

Although events were analysed by the ten categories listed above, the frequencies in each category were too small for meaningful interpretation.

Discussion

In view of the limitations of earlier studies of life event stress in relation to both schizophrenia and hypomania, the present study used the best available methods for measuring life event stress (the contextual threat measure) and for diagnosing the psychiatric disorders involved (DSM-III). The only prior study which used the contextual threat approach was that of Leff *et al* (1983), but their findings were limited by the life events rater not having been blind to the patient's clinical status (i.e.

whether or not the patient was a relapser) and by the study having been restricted to assessing relapse in a limited group of patients—i.e. those taking major tranquillisers and living with high expressed emotion families. Our study differed from theirs in a number of ways. Firstly, the life events rater was blind to the subjects' clinical status. Secondly, life events were assessed more extensively, with a larger range of time periods before onset in which events could be considered causal, different event categories, and an 'extra long-term' rating of threat. Finally, the relationship of chronic difficulties to onset was assessed. In all analyses those events and difficulties rated as dependent on the psychiatric illness in question were excluded.

In terms of diagnostic criteria, this study is the first to assess life events in relation to DSM-III criteria. Atypical psychoses and schizoaffective disorders were excluded due to small numbers. We did not intend to look at life event stress in brief reactive psychoses because of the inherent tautology: one criterion for diagnosis includes the presence of a significant stressor, but even so the number of such cases in the present series of 'functional non-depressive psychoses' was small.

However, there are two limitations to the present study. Firstly, the number of subjects in each group was small (and yet some important significant findings emerge). Secondly, patients were diagnosed by different clinicians, using clinical histories rather than structured interviews. The latter procedure might have been preferable, but was not logistically possible.

The most important findings are those for patients with schizophreniform psychosis: these had more events of long-term threat (ratings 1 and 2) over the 26 weeks prior to onset of disorder than either their matched controls, hypomanics, or schizophrenics. These differences do not appear to be attributable to sociodemographic differences between the schizophreniform patients and other subjects, and are particularly significant given the small sample size. In addition, it is important that the control groups comprised a proportion of surgical patients, in whom stressful events might be more common than in healthy subjects. The present findings do not confirm the very close proximity of precipitating life events to onset of illness reported by Brown & Birley (1968), but they do support the hypothesis that stressful events are a factor affecting the onset of schizophreniform psychosis.

In the schizophrenic patients the rate of threatening events over the 26 weeks before onset was comparable to that for age and sex-matched controls, although in the four weeks before onset three times as many schizophrenics as controls had experienced a threatening event. This difference was not significant, due to the small numbers of events and of subjects. The tendency, however, for events to be more likely to precipitate schizophreniform psychosis than schizophrenia lends some support firstly to the clinical notion that briefer psychoses are more likely to be stress-related, and secondly to the diagnostic differentiation of schizophrenia and schizophreniform psychosis. Similar but not significant trends were observed for hypomanics, with the proportion of patients having threatening events being twice that of the controls.

There is thus some indication that stressful events may precipitate schizophrenia (DSM-III). For hypomania the suggestion is a little stronger, with such patients being twice as likely as controls to have had threatening events. On the other hand, the evidence for schizophreniform disorder is strong, with stressful events being six times more likely in scuch patients than in age and sex-matched controls. A need for further research, using this advanced method on larger samples, is indicated.

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Rhoderic K. Chung, MB, BS
Pauline Langeluddecke, PhD
*Christopher Tennant MD, MPH, MRCPsych, MRANZCP, *Associate Professor*

Professorial Psychiatric Unit, Royal North Shore Hospital, St Leonards, NSW 2065, Australia.

*Correspondence

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The Epidemiology of Life Events and Long-term Difficulties, with some Reflections on the Concept of Independence

P. McC. MILLER, C. DEAN, J. G. INGHAM, N. B. KREITMAN, S. P. SASHIDHARAN and P. G. SURTEES

A total of 576 women aged 18–65, drawn from an area in Edinburgh, were interviewed. Data on life events and long-term difficulties over a six-month period prior to interview were gathered and classified according to area of life, the Bedford system, the Edinburgh system, and the independence of the event or difficulty from the subject's own actions. The highest rates of Bedford system 'provoking' situations were found in the working class, among those not employed, among women with three or more children under 14, and in the separated, divorced, widowed or cohabitating group. Similar findings emerged for hopeless situations involving choice or loss. Dependent situations were four times more common in the youngest group than the oldest, and showed a high rate among those divorced, separated, widowed, or cohabiting. It is suggested that both dependent and independent life situations should be studied.

In a previous study (Surtees *et al*, 1983) data concerning the prevalence of psychiatric disorder in Edinburgh women according to different diagnostic criteria were reported, and associations between disorder and four demographic variables set out. The present paper describes similar data on life events. Our secondary aim was to examine the concept of independence of events (Brown & Harris, 1978).

Various methods of classifying life events are available. The main issues are reviewed by Paykel (1983), Dohrenwend & Dohrenwend (1978), and Brown (1974). In this paper we classify life events in four main ways: according to a description of the area of life in which the incident occurred; according to the contextual threat/degree of difficulty methods advocated by Brown & Harris (1978); according to the approach used by Miller & Ingham (1983); and on independence as described below.

We included the first method because of its inherent simplicity and familiarity. It is of interest to know the rate of deaths, accidents, and health problems before proceeding to less familiar and more complex categories of events. There is every reason to expect associations between psychiatric morbidity and some of these categories. Deaths, for instance, are 'exits' in Paykel *et al's* (1969) classification and 'losses' in Finlay-Jones & Brown's (1981) classification. In general, the association of death with depressed mood is well documented. Accidents to children and psychiatric illness in the mother are related (Brown & Davidson, 1978) while marital problems and illness also occur together (Ilfeld, 1977).

The life event methodology of Brown & Harris (1978) at Bedford College is well known, and has been applied in a number of studies (e.g. Brown & Prudo (1981), Campbell *et al* (1983), Costello (1982), Leff *et al* (1983), Miller & Ingham (1983), Murphy (1982), Ndetei & Vadher (1981), Parry & Shapiro (1986), Surtees & Ingham (1980), and Tennant *et al* (1981). We used it with minor modifications. In the present paper we report the rates of severe events and the rates of major long-term difficulties. The main advantages in the Bedford approach are two-fold: firstly, the careful separation of the situational characteristics of an event and the subject's reaction to it; and secondly, the attempt to describe and measure the precise meaning which each event or difficulty would have for the average person.

In the MRC Unit for Epidemiological Studies in Psychiatry an effort has been made to refine the measurement of meaning by introducing new dimensions, applicable to any event or difficulty (Miller & Ingham, 1983). These dimensions are choice of action, uncertainty of outcome, hopeless situation, and anti-social act. In addition, the Bedford threat/degree of difficulty measure is divided into personal loss and threat.

A fourth way of classifying the data is on independence (Brown & Harris, 1978). This method refers to the extent to which the subject herself brought about the situation. This has been held to be important in studies concerned with cause and effect, because an event which is dependent on the subject's behaviour might be the result rather than the cause of psychiatric disturbance.

Method

Selection of sample

This has been described in detail by Surtees *et al* (1983). Briefly, a random sample was chosen consisting of women aged 18–65, drawn from a contiguous area of North Edinburgh which yielded a high proportion of working class respondents. The refusal rate on initial contact was 27%, but it was shown that despite this high rate the sample was probably not biased either in terms of social class or psychiatric morbidity. Two of the original 576 subjects had to be discarded because of incomplete life event data.

Selection and training of interviewers

A team of 22 female interviewers was recruited and given six weeks' training. Fifteen had a formal qualification in either social work, marriage guidance counselling, nursing, or teaching, while the remainder were experienced market research interviewers. Only three interviewers had less than two years' interviewing experience. Six had taken part in a pilot study, and had already received some life event training. For the remaining 16 the training began with a half-day introductory session. The group was then split into two, and each half received a further two life event training sessions. The two halves were then subdivided again into groups of four interviewers, and four more sessions were given to each group.

The training consisted of an explanation of basic life event terminology, an introduction to the two life event rating manuals—the Bedford manual and the Edinburgh manual—and practice on each other at eliciting, recording and scoring life events and difficulties. A social contacts questionnaire and a coping questionnaire were explained, demonstrated and practised. Each trainee tried out all three of these sections on at least one friend during this period. The six pilot study interviewers each joined one of the small groups of four for the last two sessions of this training. This part of the course lasted three weeks.

During the next two weeks each of the 16 newest trainees was expected to complete an interview on a friend, an interview in the community supervised by one of the pilot study interviewers, and a community interview supervised by a staff member. The completion of this task took longer than two weeks in some cases, and some interviewers had to be given extra training interviews.

Training included a simulation exercise. An actress role-played two different people with carefully chosen life events. Pairs of interviewers took turns to conduct a life events interview. One interviewer in each pair therefore interviewed 'Mrs A' (while the other observed), then the other interviewed 'Mrs B'. Any obvious faults in interviewing technique during the session were then pointed out. Each interviewer rated both role-play interviews, decided what events and difficulties were present, and scored these according to the manuals.

A final exercise was then given in which each interviewer practised some of the ratings on the written records of five of the most complex cases from the pilot study.

All the interviewers performed satisfactorily on these tasks, although some had to do extra community interviews. They were being trained simultaneously on methods of rating psychiatric morbidity (see Surtees *et al*, 1983). One interviewer failed to complete that aspect of the training satisfactorily and did not take part in the survey.

The interviewers were monitored throughout the fieldwork. They showed their written records of all interviews to one of two staff members, available to examine and resolve ambiguities. In a few cases the interviewers went back to obtain further information from the subjects.

Life event interview and rating methods

The interview method was derived directly from the Bedford interview method (Brown & Harris, 1978), but differed from it in two small ways. Firstly, the method of recording the interviews was note-taking, backed up by tape-recordings in one tenth of the cases. Secondly, the initial method of eliciting life events and difficulties was by a list which the subject ticked, rather than by a set of questions asked verbally. The interviewer then probed each putative incident carefully, obtaining all the relevant contextual material.

Each interviewer made an initial attempt to score each interview, and this was checked over by a staff member. The design of the survey required most of the subjects to be seen three times at six-monthly intervals. Although this paper is concerned only with the first of these interviews, the main life event scoring was performed on all the available completed interviews for each subject. When the survey was over, two staff members and three of the interviewers worked in pairs to review and score the material again. For most subjects this covered 18 months, but for some it was 12 or 6 months. Occasionally, data obtained at later interviews resulted in revision of the ratings made on the basis of first interview data only. This was particularly true for long-term difficulties.

The raters first divided the material into events and long-term difficulties, using Bedford criteria (these criteria were adhered to strictly, and were not relaxed as in the Livingston survey (Miller & Ingham, 1983)). They then made several ratings on each situation (either an event or a long-term difficulty) present.

The dates

For events, these were measured to the nearest week prior to interview. For long-term difficulties two dates were recorded, one reflecting its starting date and one its finishing date. For difficulties of less than two years' duration the starting date was measured to the nearest week prior to interview. For the rest, it was estimated to the nearest year.

A large number of difficulties fell into the category 'still going on'. For those that had ended, the finishing date was given in weeks prior to interview.

Independence ratings

This series of ratings sought to give a clear picture of the extent to which a subject was herself responsible for a situation. Our development of the concept introduced by Brown & Harris (1978) needs some elaboration. We applied independence ratings both to events and to difficulties, and we evolved a four point scale. An event or difficulty was considered to be dependent if the subject's own actions at any time during the 18 months could have seriously influenced our other ratings on it (threat, choice, uncertainty, etc.). To arrive at a rating we first assessed the event or difficulty itself, deciding whether (a) the subject could have caused it to occur and (b) whether the subject's actions following the incident could have made its consequences worse. For long-term difficulties which started outside the period, rating (a) is not applicable. Rating (b) is only occasionally important for events. For example, an office worker was asked by her boss to help move furniture. She refused. There was a row which ended with the resignation of another office worker (not the boss or the subject). We felt that although our subject possibly did not cause the trouble in the first place she certainly made the furniture removal into an event, and we rated it as dependent. Rating (b), however, applies much more frequently to long term difficulties. For instance, we consider most marital difficulties to be dependent under this head. However little the subject may have contributed to starting the difficulty, her actions will clearly be likely to influence whether or not it becomes major. Ratings on (a) and (b) were made on a four-point scale ranging from probably dependent to probably independent.

Having assessed the event or difficulty itself, we then considered whether it was directly linked to another event or long-term difficulty which occurred prior to it within the period. If it was, we made ratings (c) and (d) of this prior incident analogous to (a) and (b) for the situation itself. A simple example of this concerns birth events. A birth (or miscarriage or termination) is inevitable given that the subject has become pregnant. However, becoming pregnant is in most cases a dependent event, and this means that in most cases the birth will also be taken as dependent. We applied this 'prior initiation' rule to births to the subject, regardless of whether knowledge of pregnancy was inside the period of time we were covering. In all other cases, if a prior initiation came before the start of our time period we disregarded it; to do otherwise would have involved looking at situations which might have occurred several years prior to interview. Our ratings of dependence therefore concern the extent to which the subject influenced the situation within the time period over which we followed her. The rating assigned was the most dependent out of (a), (b), (c) and (d).

Interaction changes

This series of ratings concerned situations involving exits and entrances from the social field. Where important people died or moved away it was recorded who this was. Other ratings designated people who entered the social field, and indicated whether the situation involved an impaired relationship with an important person and whether there were changes in more superficial support.

Bedford ratings

The short-term threat/long-term threat and focus of each event, and the objective and general severity of each difficulty (Brown & Harris, 1978), were rated.

Edinburgh ratings

The six ratings developed and described by Miller & Ingham (1983) were applied to both events and difficulties. Choice of action (C) was scored for an event when, one week after the event occurred, the subject still had an important choice to make. Hopeless situation (H) was recorded when, a week later, all the foreseeable outcomes of the event have been or will be bad. An anti-social act (A) was present when some form of authority was involved against the subject or people close to her. Uncertainty of outcome (U) occurred when on the day of the interview there was an important aspect of the situation unresolved. Finally, events which scored 1 or 2 on Bedford threat were automatically scored threat (T), or loss (L), or both. An L score was assigned only if the event involved an important exit from the social field. Losses of property or of cherished ideas (e.g. career aspirations, a spouse's love) were not scored L (c.f. Finlay-Jones & Brown, 1981). Both L and T were scored where there were threatening implications apart from personal loss. For long-term difficulties analogous ratings were made (a manual is available from the authors).

Area of life

The area of life in which the situation occurred (e.g. marital, housing, money) was recorded. We used a pre-structured list of areas with 12 headings. It is often possible to classify a situation under more than one heading; we took the one which seemed to be the most salient.

Tag rating

This shows which other situations might have caused or been caused by the situation being rated.

From the Bedford ratings, following Brown & Harris (1978), we assessed whether or not each situation was what they term a provoking agent. This was defined as either an event scoring 1 on long-term threat, or a subject-focused event scoring 2 on long-term threat, or a long-term difficulty which was present for at least two years, scored 1, 2 or 3 on degree of difficulty, and was not a health difficulty.

Following previous work (Miller & Ingham 1983), we made one further classification on the basis of the Edinburgh ratings. This is again a dichotomy, in which situations which scored hopeless (H) and either choice (C) or loss (L) were assigned into the positive category and the rest into the negative. The previous finding was that hopeless situations with choice or loss were particularly likely to be associated with depressed mood.

Results

Table I sets out the rates found for events and long-term difficulties, classified in seven different ways. This is a selection from the categories described above. The full breakdown of events and difficulties according to the Edinburgh classification system is given in the Appendix. Breakdowns of situations classified as family relations, money, housing, children, legal, death, accident and other may be obtained from the authors.

The 'all situations' column is not the sum total of the other columns, because the latter are only a selection of the ways in which situations are classified. Some of the classifications are mutually exclusive; for example, a neutral/pleasant situation cannot be provoking or hopeless with choice or loss, and work, health and marital situations are mutually exclusive.

The majority of events and difficulties are moderately independent (i.e. rated 3 or 4 on independence). Of the categories in Table I, health shows the highest proportion of independent situations; the subject plays little part in bringing about illness. Health situations regarded as dependent concern pregnancy, gambling, alcoholism and drugs. The most dependent group of situations is the group scored hopeless with choice or loss. This is because any situation scored as choice of action stands a high chance of being dependent. However, it should be noted that it is not necessarily so; for events, choice is rated seven days after the main incident. For example, a whole firm could suddenly close down (independent event), creating a choice for the subject of taking another, poorer, job or emigrating. For long-term difficulties it may happen that, although the difficulty started outside the period and is basically intractable (independent), there are still important week-to-week choices to be made (e.g. which bills to default on in a severe money difficulty). Since the rates shown are for six months, the event rates per annum would be expected to be about double those given; the long-term difficulty rates would be much less than double, because the majority of long-term difficulties had lasted for several years prior to interview.

Figure 1 shows how some event types were distributed over time. Only for the neutral/pleasant events does there seem to be a reduction in rate when moving backwards in time from the day of interview.

Tables II-V show the social class, employment, age, and marital status tabulations of the seven categories of Table I. For these tabulations the event and long-term difficulty rates taken separately show broadly similar patterns, and therefore in the interests of brevity and of larger numbers we have combined events and difficulties (and use the term 'situation' to describe both). Tables with events and difficulties separated may be obtained from the authors.

Table II shows that working and middle class women differ only on independent situations, with the working

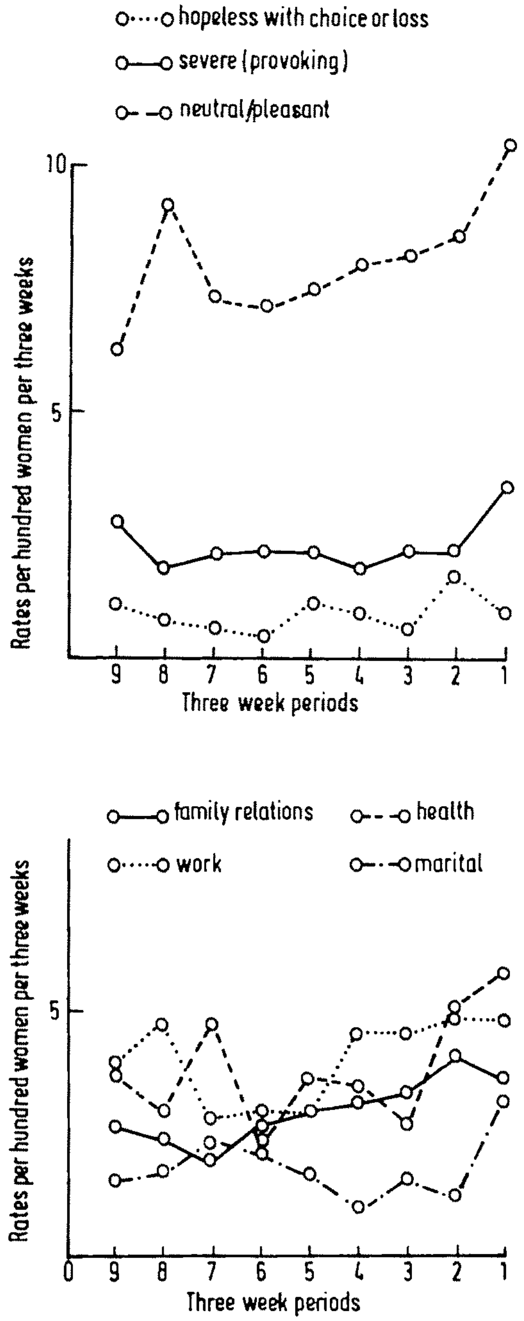

FIG. 1 Rates of events by time before interview. Period 1 covers from 4 days prior to interview to 3 weeks 3 days prior. In the 3 days immediately prior to interview the rates were: severe events 0.2, hopeless events with choice or loss 0.0, neutral events 1.2, family relations 0.5, work 1.2, health 0.9, marital 0.0.

TABLE I

Rates per 100 subjects per six months of moderately dependent and moderately independent[1] events and long-term difficulties classified in different ways

	All situations	*Work*	*Health*[2]	*Marital*[3]	*Provoking*[4] *situations*	*Hopeless situation with choice or loss present*	*Neutral/pleasant situations*
Moderately dependent events	64.1	16.7	5.1	14.5	7.7	2.1	30.0
Moderately independent events	101.9	19.0	28.8	1.2	11.3	5.1	41.5
Moderately dependent difficulties	50.4	5.8	4.4	13.4	10.8	16.7	0.7
Moderately independent difficulties	143.9	16.7	90.9	0.9	14.3	16.7	3.3
Total	360.3	58.2	129.2	30.0	44.1	40.6	75.5

1. Moderately dependent = points 1 and 2 on the independence scale; moderately independent = points 3 and 4
2. Health includes alcoholism, pregnancy, gambling, drugs
3. Marital includes boyfriend/girlfriend/cohabitee relationships, and also births to the subject
4. Provoking events are those scoring 1 on long-term threat and those which are both subject-focused and score 2 on long-term threat. Provoking difficulties score 1, 2 or 3 on degree of difficulty, have been going for 2 years or more and are not concerned with the subject's own health

TABLE II

Rates per 100 subjects per six months of various types of situation in middle and working class women[1]

	All situations	*Work*	*Health*	*Marital*	*Provoking situations*	*Hopeless situation with choice or loss present*	*Neutral/pleasant situations*
Middle class ($n=336$)							
Moderately dependent	113.1	23.8	7.7	30.1	15.5	13.4	32.4
Moderately independent	211.3	31.6	103.9	1.5	19.6	15.5	41.4
Total	324.4	55.4	111.6	31.6	35.1	28.9	73.8
Working class ($n=230$)							
Moderately dependent	112.6	20.9	12.2	25.2	22.2	24.4	28.3
Moderately independent	293.0***	43.0**	142.2***	2.6	33.5*	31.3**	48.7
Total	405.6**	63.9	154.4***	27.8	55.7*	55.6**	77.0

1. Eight women are excluded due to their social class being unclear

*Working class/middle class rate differs, $P<0.05$, using the Mann-Whitney U test

**$P<0.01$

***$P<0.001$

TABLE III
Rates per 100 subjects per six months of various types of situations among employed and not employed women

	All situations	*Work*	*Health*	*Marital*	*Provoking situations*	*Hopeless situation with choice or loss present*	*Neutral/ pleasant situations*
Employed ($n=407$)							
Moderately dependent	113.8	25.1*	7.4	29.0	16.2	17.0	33.7
Moderately independent	222.9	31.2	107.1	2.0	20.2	19.4	45.0
Total	336.7	56.3	114.5	31.0	36.4	36.4	78.7
Not employed ($n=167$)							
Moderately dependent	116.2	16.2	14.4**	25.2	24.6*	23.4	23.4
Moderately independent	301.8***	46.7	150.3***	2.4	38.3*	27.5	44.3
Total	418.0***	62.9	164.7***	27.6	62.9**	50.9	67.7

*Employed/not employed rate differs, $P<0.05$, using the Mann–Whitney U test
**$P<0.01$
***$P<0.001$

TABLE IV
Rates per 100 subjects per six months of various types of situation according to age

	All situations	*Work*	*Health*	*Marital*	*Provoking situations*	*Hopeless situation with choice or loss present*	*Neutral/ pleasant situations*
Age group 18–34 ($n=282$)							
Moderately dependent	158.9	34.0	12.1	44.7	25.9	20.2	45.7
Moderately independent	229.4	35.1	95.7	3.6	23.8	17.7	42.2
Total	388.3	69.1	107.8	48.3	49.7	37.9	87.9
Age group 35–54 ($n=192$)							
Moderately dependent	87.0	14.1	7.8	15.6	12.0	22.4	19.8
Moderately independent	260.9	41.2	131.3	1.0	24.5	27.6	52.6
Total	347.9	55.3	139.1	16.6	36.5	50.0	72.4
Age group 55+ ($n=100$)							
Moderately dependent	42.0	6.0	5.0	4.0	11.0	8.0	9.0
Moderately independent	263.0	27.0	165.0	0.0	32.0	22.0	37.0
Total	305.0	33.0	170.0	4.0	43.0	30.0	46.0
Moderately dependent	$P<0.001$*	$P<0.001$	NS	$P<0.001$	$P<0.01$	NS	$P<0.001$
Moderately independent	$P<0.05$	NS	$P<0.001$	$P<0.05$	NS	NS	NS
Overall	$P=0.05$	$P<0.001$	$P<0.001$	$P<0.001$	NS	NS	$P<0.001$

*i.e. the three moderately dependent rates for the column differ beyond the 0.001 level using the Kruskal-Wallis one way analysis of variance

TABLE V

Rates per 100 women per 6 months of various types of situation according to marital status

	All situations	*Work*	*Health*	*Marital*	*Provoking situations*	*Hopeless situation with choice or loss present*	*Neutral/ pleasant situations*
Single ($n=121$)							
Moderately dependent	128.1	27.3	5.0	38.0	14.1	13.2	33.1
Moderately independent	183.5	19.8	88.4	3.3	9.9	19.8	36.4
Total	311.6	47.1	93.4	41.3	24.0	33.0	69.5
Married ($n=348$)							
Moderately dependent	86.5	17.8	10.6	18.1	13.5	12.6	27.6
Moderately independent	251.2	43.4	130.5	1.2	25.9	19.5	47.1
Total	337.7	61.2	141.1	19.3	39.4	32.1	78.1
Separated, widowed, divorced or cohabiting ($n=105$)							
Moderately dependent	191.4	32.4	10.5	48.6	41.0	45.7	38.1
Moderately independent	300.0	28.6	120.0	3.8	41.9	31.4	49.5
Total	491.4	61.0	130.5	52.4	82.9	77.1	88.5
Moderately dependent	$P<0.001$*	$P<0.05$	NS	$P<0.001$	$P<0.01$	$P<0.001$	NS
Moderately independent	$P<0.001$	$P<0.05$	$P<0.05$	NS	$P<0.001$	NS	NS
Overall	$P<0.001$	NS	$P<0.01$	$P<0.001$	$P<0.001$	$P<0.001$	NS

*i.e. the three moderately dependent rates for the column differ beyond the 0.001 level using the Kruskal-Wallis one way analysis of variance

class having higher rates of moderately independent work and health situations. Those situations found in previous studies to be particularly associated with psychiatric illness and symptoms, i.e. provoking situations and hopeless situations with choice or loss, also have higher rates in working class women.

In Table III a similar pattern emerges between employed and not employed women. The high rate of health situations in not employed women is worthy of note, as is the finding that employed women have a higher rate of moderately dependent work situations. Many of these will be changes of job, return to work events, and minor work long-term difficulties. The event 'loss of job' may be either dependent or independent, and is not common enough to give the not employed a higher rate of work situations.

The main features of Table IV are the sharp decline of dependent situations and the large increase of health-related situations with advancing age.

In Table V we see that those who are separated, widowed, divorced or cohabiting have the highest rates for most situations, and this usually applies both to dependent and independent situations. The married group, however, have the highest rates of independent work and illness situations.

Finally, we compared the rates for the different types of life situation for women with three or more children aged under 14 at home ($n=28$) against the rest ($n=546$), and for women separated for a year from one or both parents before age 11 ($n=111$) against the remainder ($n=463$). Women with three children tended to have more situations overall ($P<0.003$) and, in particular, more of the provoking situations ($P<0.0003$; rate for women with three children $=128.6$; rate for other women $=39.7$). Those who suffered parental separation had significantly more dependent provoking situations ($P<0.005$; rate for those separated $=36.0$; rate for other women $=14.5$). These two findings were paralleled at slightly lower levels of significance in the choice-hopeless situations. There were no other significant findings.

Discussion

The 574 women in the sample have been classified in four main ways: according to social class, employment status, age and marital status. We have direct evidence (Surtees *et al,* 1983) that psychiatric illness is more common in working class women, in the unemployed, in the divorced, separated, and cohabiting group and, more tentatively, in the middle-aged group. It is of interest to describe the life events and long-term difficulties within these various groups. The direct connection between life situations and pathology will be made elsewhere. Here we simply focus on life event epidemiology, and it is necessary to remember the ecological fallacy—an excess of a particular kind of life situation within a group with high pathology does not necessarily mean that it is the people with that situation who are ill.

Our results may be compared with those of other surveys (e.g. Brown & Harris, 1978, and Surtees *et al,* 1981). The overall event rate in the present study was 166.0 per 100 women per six months. Surtees *et al* obtained 159.7 in a sample of control Livingston women, and the figure for Brown and Harris for normal women would appear to be around 150 (based on their Table 1). In neither case would results identical to ours be expected, as the samples differ in several ways, but it is nonetheless reassuring that the rates are not too dissimilar. Our results resemble those of Brown & Harris in another important respect; there appears to be little drop in event rates over time for the severe events.

The 'average' working-class woman differs from her middle-class counterpart in several interesting ways. Most importantly, she suffers a greater rate of independent situations—i.e. she seems to play a lesser part in controlling her circumstances. Many of these situations, in particular those labelled provoking and the hopeless ones with choice or loss, will be thoroughly unpleasant. Her physical health is on the whole worse than that of a middle-class woman. However, marital situations are similar in the two groups, and the excess of provoking situations is in other areas of life such as work and health.

Women who are not employed show relatively few differences from those who are, but they do suffer a higher rate of provoking situations. Much of the excess is dependent—i.e. the woman might have played a part in bringing about the situation. In some cases this may reflect loss of job, but there is no significant difference in work situations. Indeed, in dependent work situations the difference is the other way round—the employed showing the higher rate. Some of the excess may be reflected in severe illness events.

The most interesting difference according to age is that younger women have a large excess of moderately dependent situations—nearly four times the rate of the 55+ age group. They tend to make things happen, while older women have things happen to them. This extends to provoking situations, to work situations, to dependent health situations (mostly pregnancy), to marital/boyfriend situations, and to neutral and pleasant ones; in all of these categories there is a clear trend to decrease with age over the three age groups. Independent situations show no such trend, and not surprisingly there is an exact reversal for independent health situations—older women having nearly twice the rate of women under 35.

The separated, divorced, widowed, and cohabitating group have higher rates in most categories than married and single women. They find themselves in threatening and difficult situations, many of which they have themselves instigated, and some of which require harrowing choices to be made. They have the highest rates of marital/boyfriend and dependent work situations. On average, each woman in this group will have suffered a provoking situation of some kind in a six month period. In this respect the results are similar to those of Perris (1984), who conducted an epidemiological study in a sample of 204 patients suffering from depressive disorder. Perris rightly points out that many of the events suffered will be those that classify the subject into the divorced, widowed, separated or cohabitating group.

We differ from Perris in the results on age. He found his 'independent events' to decrease with age, whereas we found that only the dependent situations did so. However, his definition of an independent event is quite different: many events which he designates as independent would be most unlikely to be so in our terms (e.g. 'moved to another house', 'married or started living in partnership', 'started working', 'got a baby', 'other types of trouble within the family').

That some groups of women are more event and difficulty-prone than others comes as no surprise. Indeed, it is perhaps a truism. Further, as Cooke (1981) has suggested, the study of life events may to some extent be a doomsday exercise. There is little that can be done, so the argument runs, to prevent the occurrence of severe life events. However, this may not apply to the more dependent life situations. It may make good sense to ask whether there is an event-prone personality, and, if so, whether any intervention is necessary or desirable. Even 'independent events' and long-term difficulties may sometimes be caused in subtle ways by the subject herself. For example, her husband goes to work and suffers a car crash—did she irritate him in some trivial way before he left and thus impair his concentration? Again, a dependent event in the distant past, such as marrying an alcoholic, or failing an exam at university, might place the subject in an environment where independent events are more common.

The concept of an independent event was originally introduced to try to help establish the direction of causation. By ruling out the possibility that an incipient psychiatric illness might have led the subject to have instigated the event before becoming clinically ill, it was argued, one source of circularity had been removed. As will be realised, we have some doubts about this; not because the argument is unsound, but because it is difficult to be sure that an event is truly independent. Evidence is accumulating (Ingham & Miller, 1984) that the transition from being well to being ill is frequently from a state of mild to a state of somewhat more severe symptomatology. Some people have multiple episodes, with states of remission in which some symptoms are still present. Few subjects seem to have been tested at the time of their first episode of illness. Under these circumstances it seems entirely possible that many of the so-called independent events might have been open to influence in subtle ways.

There are two further reasons for concern. Firstly, excluding dependent events and difficulties from consideration inevitably biases the sampling of life situations. Most marital rows and family difficulties, for instance, would be excluded, and a high proportion of physical illness difficulties would be included. The attempt to exclude dependent situations would thus result in a sample of situations whose characteristics had changed in other dimensions than just the dependent-independent one. This

TABLE VI

Frequencies of different types of events and long-term difficulties over a six month period. (n=574, total no. of situations=2068)

Classification	*Events*	*Long-term difficulties*	*Classification*	*Events*	*Long-term difficulties*
CUHLT[1]	—	1	CH	8	99
CUHAT	1	4	HT	22	81
CUHT	2	7	CU	11	59
CHLT	1	—	CT	14	38
CULT	1	—	UT	12	14
CHAT	1	5	UH	7	11
UHAT	2	—	HL	14	—
CUHA	1	1	CL	7	—
CHT	9	68	CA	6	2
UHT	5	16	LT	2	1
CUT	3	23	AT	6	1
CUL	1	—	UA	1	—
HLT	1	1	HA	3	5
CHL	1	1	C	65	135
CLT	2	2	U	26	44
HAT	3	1	H	33	336
CAT	—	3	L	8	—
CUA	2	2	A	16	1
UHA	1	—	T	45	14
CHA	1	1	Minor threat only	198	111
CUH	—	4	Neutral and pleasant	411	23

[1] C=choice of action, U=uncertainty of outcome, H=hopeless situation, L=personal loss, A=anti-social act, T=threat

must affect the generality of any conclusions drawn. The second reservation concerns the concept of causation implied. If the aetiology of tuberculosis was under investigation would one really deny the causal influence of the TB bacillus, if the subject had deliberately exposed herself to it?

Brown and his co-workers, however, have made it clear that they never intended to imply that dependent events could not cause illness (Brown & Harris, 1982). The question of whether dependent and independent situations differ in their effects is interesting in its own right, and the origins of dependent events are also worthy of investigation. For example, there is a strong hint that early parental separation may be associated with life situations classified as dependent and provoking in later life. Other variables (e.g. coping ability, neuroticism, locus of control, extraversion-introversion) which might be associated with dependent events easily suggest themselves. Further study of these matters might result in a better understanding of the process of becoming ill.

Appendix

Table VI shows the frequencies of events and difficulties with the various combinations of characteristics. They are reasonably similar to those found on the Livingston survey (Miller & Ingham, 1983), with two main exceptions. The combination UH is less frequent throughout the table (i.e. there are fewer CUHT situations and more CUT and CHT). The other exception is that loss (L) is much less frequent. There are three possible reasons. Firstly, there were small changes in our rating methods, improving reliabilities. Secondly, the samples differed. In Livingston a large proportion of subjects were men, there were more working class subjects, and a larger proportion were selected because they were showing symptoms of depression and anxiety. Thirdly, the time period in Livingston was only three months, as against six months in Edinburgh.

Our reliabilities for the characteristics, as measured by Maxwell's RE coefficients on a random sample of 25 subjects, were C=0.76, U=0.72, H=0.79, L=0.96, A=1.0 and T=0.72.

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*P. McC. Miller, BSC, PhD, *Member of the Scientific Staff*

C. Dean, MB, ChB, BA, MRCPsych, *Consultant Psychiatrist, Manchester Royal Infirmary, Manchester 13*

J. G. Ingham, BSc, PhD, FBPsS, *Assistant Director*

N. B. Kreitman, FRCP(Ed), FRCPsych, MD, *Director*

S. P. Sashidharan, MB, BS, MPhil, MRCPsych, *Member of the Scientific Staff*

P. G. Surtees, BSc, MSc, PhD, *Member of the Scientific Staff*

MRC Unit for Epidemiological Studies in Psychiatry, University Department of Psychiatry, Royal Edinburgh Hospital, Morningside Park, Edinburgh EH10 5HF

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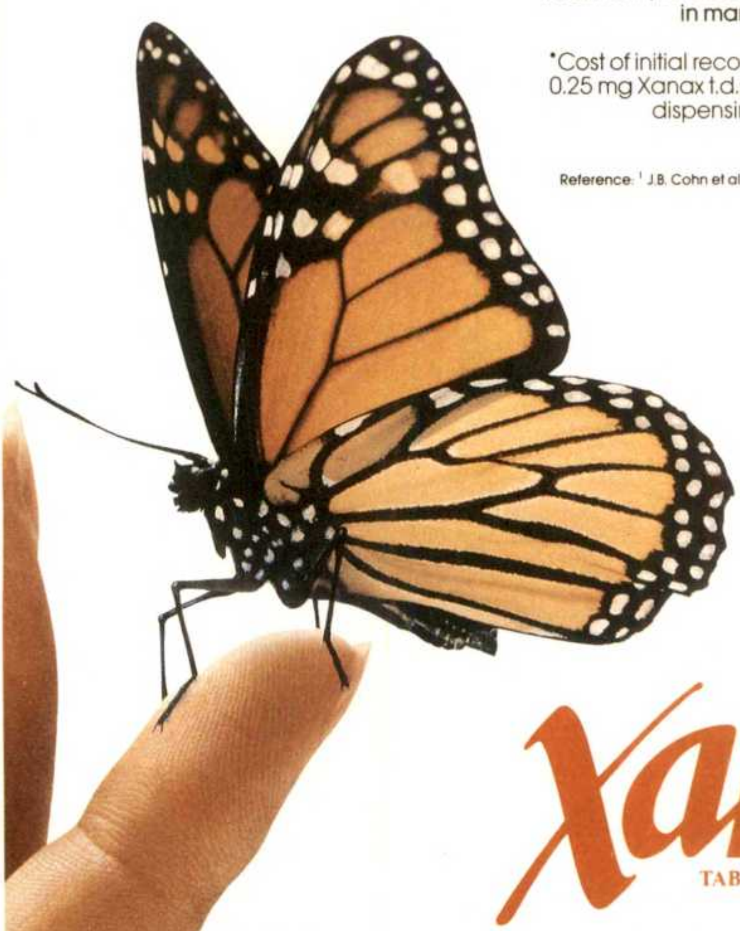

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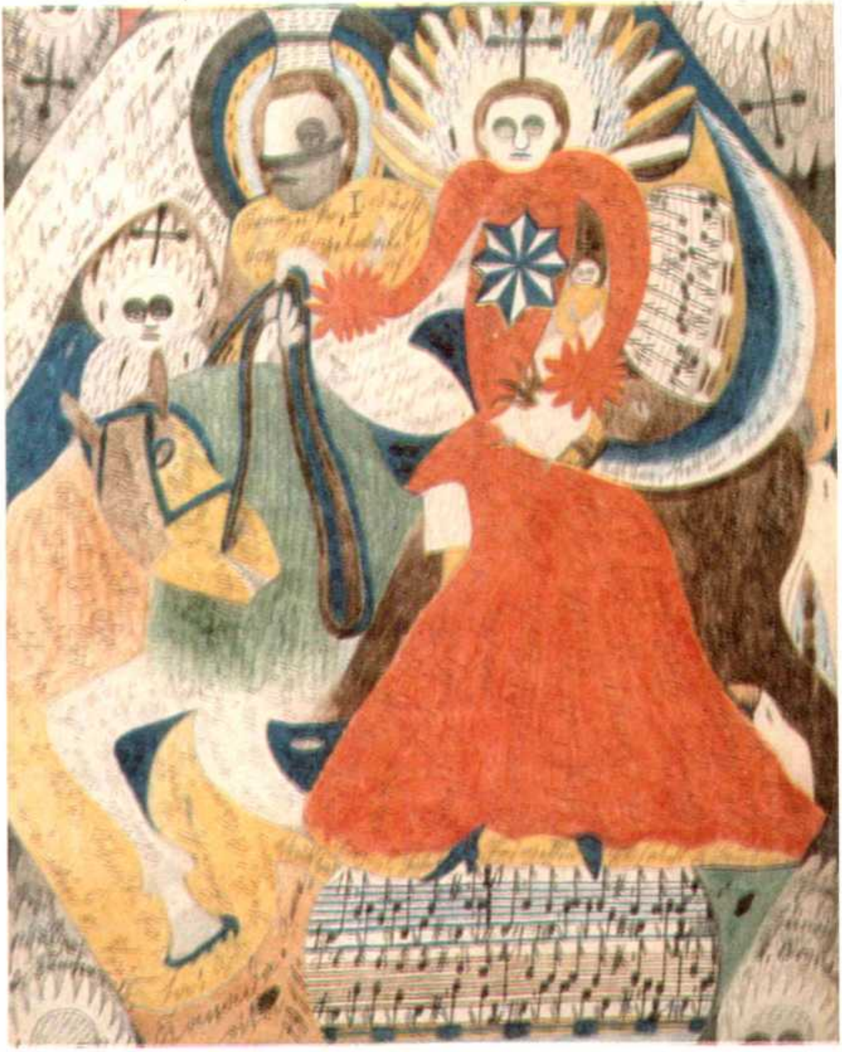

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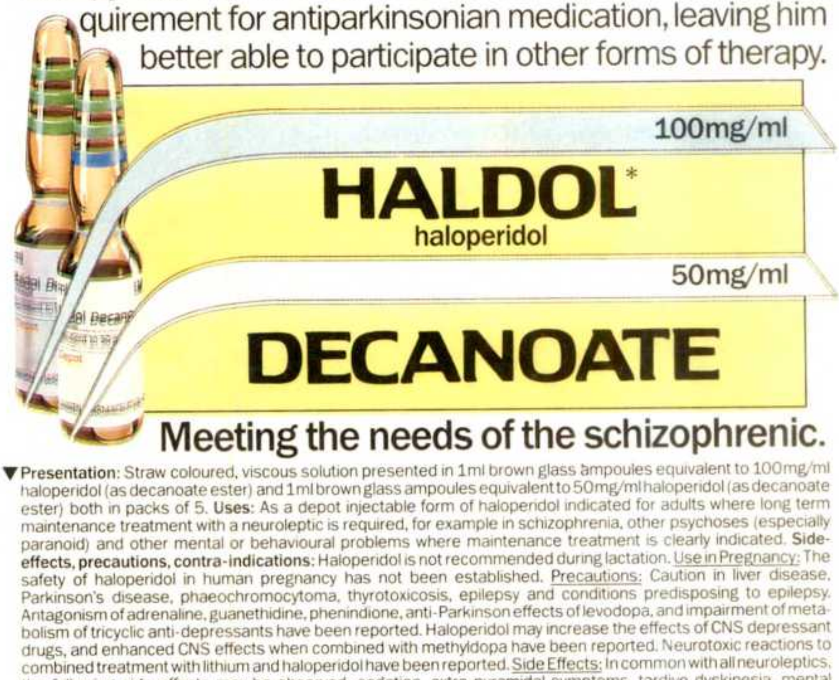

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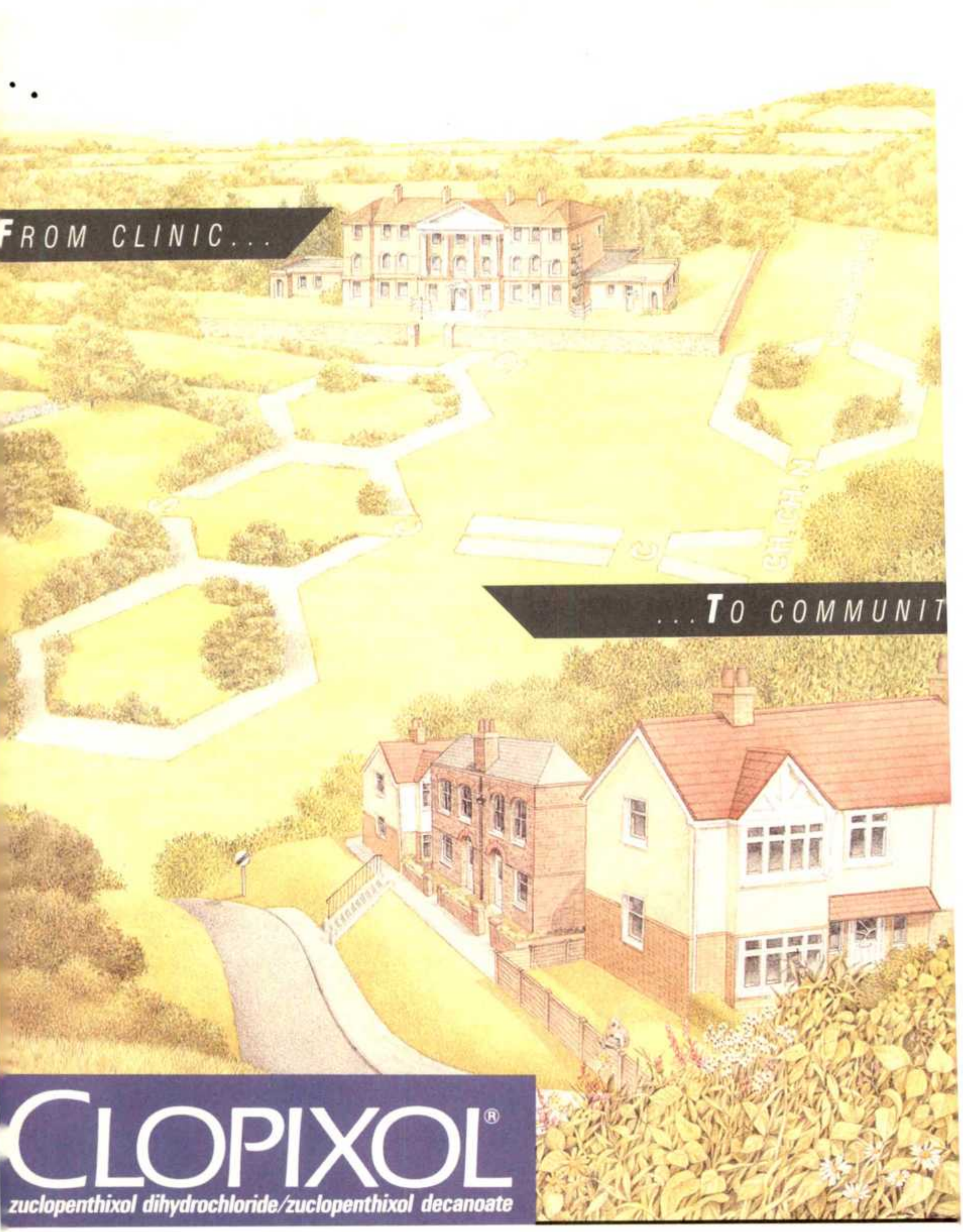

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Alcoholism and the General Practitioner

ALISON MOWBRAY and NEIL KESSEL

Fifty-three urban general practitioners were questioned about alcoholism. They mostly had reasonably good, if sometimes muddled knowledge of the condition, when to suspect it, and how to confirm its presence. Social harms were seen as predominant over somatic ones. The majority had had postgraduate instruction supplemented by reading. Most were prepared to treat alcoholics, and revealed tolerant and sympathetic attitudes towards them and their families. The survey negates the general impression of unwillingness by general practitioners to engage with alcoholism.

A major role has been suggested for general practitioners (GPs) in treating alcoholics (DHSS Advisory Committee on Alcoholism, 1978) and they are certainly in a key position to detect it. Yet doubts have been widely expressed about their competence and willingness to detect it to perform either task. Thus in the one British study that offered survey evidence Rathod (1967) analysed postal questionnaire responses from GPs and reported that 28% regarded moral weakness, vice, bad habit, etc. as most appropriate to describe alcoholism, while 21% thought such terms moderately appropriate. Jones & Helrick (1972) found that American GPs thought similarly. Wilkins & Hore (1977), in a low response study, commented on 'the GP's lack of confidence in his knowledge of the alcoholics in his practice'. Recently, while alcoholism continues to be on the increase, there has been commendable educational effort by the DHSS itself, by Universities and Royal Colleges, by the Medical Council on Alcoholism and also in the public media, designed to increase awareness of, interest in and information about alcoholism. We decided therefore to examine the current position.

Method

The study was carried out in Manchester and Bolton. We report the responses of principals in general practice who were personally interviewed about their knowledge of alcoholism and their alcoholic patients, about their attitudes and about their skills and practices. Interviews were unstructured, except for the written presentation of a number of attitude statements calling either for agreement or disagreement. Pilot interviews had proven the understandability of the questions. The 86 GPs we approached were available from 114 GPs selected by random sampling from local lists; 28 had left, were on holiday or ill. Of these, 33 told us that owing to their partners being on holiday during the summer months of 1984 when the survey had to be conducted, they were too busy, so that 53 were interviewed. Of these 47 were male and 16 had qualified overseas; four had been qualified for less than 10 years, 16 between 10 and 20 years, and 33 even longer; six had been in their present practices for less than five years.

Results

How they knew about alcoholism

Two doctors denied any knowledge of alcoholism; the subsequent responses of one rather confirmed his claim. Twelve (23%) remembered instruction as medical students; 31 (58%) had received postgraduate teaching; 39 (74%) had gained knowledge by reading, chiefly the old British Journal of Alcoholism that used to be distributed free to all GPs; 45 had learned from their experience in dealing with alcoholics; and for five, this was their only source of knowledge.

Definitions

Twenty-two (42%) regarded alcoholics as separate from problem drinkers: the distinguishing feature was whether or not there was dependence. Thirty-one (58%) made no such differentiation; of these, 18 proffered a definition of alcoholism such as 'where alcohol controlled the person', and this included dependence. Six others relied solely on excessive consumption, five only on the presence of alcohol-related problems, mostly social, but including dependence, and two ventured no definition.

Extent of alcoholism among their patients

We asked each GP to estimate the number of patients, either on his own list or, if it was more realistic, in the practice, divided by the number of principals. Knowing list sizes, we have converted these estimates to prevalences (Table I). The commonest rate cited was between 2 and 3 per 1000, but one GP owned to no alcoholic patients. These figures are useful chiefly for comparison with an estimate of 10 per 1000 derived from a rough but widely accepted guess of 500,000 alcoholics in England and Wales. The prevalence could well be higher in these urban

TABLE I
Prevalence estimates

Alcoholics per 1000 patients	*Number of GPs*
0	1
<7.5	34
7.5–15	9
16–35	9

practices, so that even allowing that some alcoholics may be unregistered, most GPs were aware of less than their practices contained; 70% said they were seeing more alcoholics than 10 years ago, but were not sure whether this represented better identification or a true increase. Although half the doctors thought that the average age of alcoholics was lower now than 10 years ago, 19 GPs knew of no alcoholics below the age of 35 and, of those who did, 85% thought there were not many below that age. Only one knew of an alcoholic aged under 20. Thirteen GPs (25%) did not think there were more male than female alcoholics; indeed, two thought women alcoholics outnumbered men. Although the prevalence of alcoholism in women is rising it is surprising to find such assertions.

The main problems associated with alcoholism

Table II shows that GPs regarded social problems (marital, family, employment, finance, crime and violence) as predominating. Even those who mentioned somatic problems thought that social effects were more important; psychiatric and emotional problems were equally divided between personality defects and depression. The final category included the problem of patients not accepting that there was a problem, their lack of motivation to change, their resistance to being helped and their tendency to relapse.

Half the GPs thought that alcoholism was associated with heavy smoking and one-third associated it with abuse of prescribed drugs, chiefly minor tranquillisers. Only 10% linked it with illicit drug taking. One-third of the GPs did not think any other addictions were associated.

TABLE II
Main problems associated with alcoholism

Problem	*Percentage of GPs mentioning it*
Social	68
Somatic	45
Psychiatric and emotional	25
Denial, lack of motivation, relapse	28

TABLE III
(a) Conditions or presentations raising suspicion of alcoholism

	Percentage responding		
	Always	*Sometimes*	*Rarely or never*
Gastritis	45	49	6
Pancreatitis	43	42	15
Impotence	47	40	13
Family violence	75	21	4
Monday morning absenteeism	55	34	11

(b) Other ways of becoming aware

Percentage of 53 doctors mentioning each item	
Told by family	49
Heard from other sources	28
Report from hospital	23
Domestic or family breakdown	15
Accident or trauma	8
Signs observed during consultation	57

What aroused suspicion of alcoholism

It was the rule for alcoholics to consult, ostensibly for other reasons. The 52 doctors who knew of alcoholic patients all said they regularly met alcoholics who consulted them in this way. Besides this, the majority of GPs (33) said that some patients whom they knew to be alcoholics had not consulted at all.

Table IIIa shows the extent to which GPs considered a diagnosis of alcoholism when presented with certain somatic and social factors. Unassociated conditions, such as diabetes, which we included in our list, were rejected by almost all doctors. Three-quarters always considered alcoholism in instances of violence in the family; only a half did so as a matter of course when faced with other factors, but nevertheless they were well aware of the possibility of an alcoholic aetiology. Many factors besides the presenting complaint alerted GPs (Table IIIb). Clearly, information from family or outside sources is important. The alerting signs observed during a consultation were: neglected appearance, breath smelling of alcohol, slurred speech, plethoric complexion, suffused conjunctivae and coarse tremor.

How suspicions were confirmed

Once alerted, the doctor has to go further to confirm the diagnosis. Table IV outlines the enquiries made. Two GPs took no steps, one because the patients would always tell if alcohol were a problem, the other because alcoholics would conceal the truth! All the other GPs asked about the

TABLE IV

Enquiries made to confirm the presence of alcoholism

Measure	*Number of GPs*	*%*
None	2	0
Quantity and frequency of consumption	51	96
Symptoms of dependence	32	60
Other harms resulting	29	51
Laboratory investigations	10	19
Approaching a relative for information	38	72

quantity and frequency of drinking i.e. consumption; one-third asked only about this. Most sought evidence of dependence, and half enquired about other harms. Just less than half of the doctors asked about the complete trio of consumption, dependence and other harms. The laboratory investigations ordered were generally blood count, urea and electrolytes, and liver function tests. Three-quarters of the GPs said they sometimes approached a family member for confirmation; it was something of a surprise that a quarter rarely or never took this obvious step.

Embarrassment and avoiding the subject

Ninety per cent said they were not embarrassed in dealing with alcoholic patients; the remaining five doctors contained three of the six women. Nevertheless, 20 (38%) said that sometimes they did not take a drinking history, even when they thought they should. Their reasons included: the belief that it was useless since alcoholic patients 'always let you down'; a hope that the patient would change his habits spontaneously; an idea that it was better to wait to see if the problem became chronic; the difficulty of handling 'high status' patients; wishing to avoid confrontation of aggressive patients; and a feeling that the time was inopportune.

Available help and the use made of it

Eight doctors did not refer alcoholic patients to hospital; 45 referred at least some, mostly one, two or three a year. Thirty-seven sent patients to Alcoholics Anonymous, including seven of the eight who spurned hospital referral (the eighth had no alcoholic patients). Other sources of help included social workers (12 GPs), the local council on alcoholism (5), and Al-Anon (7). Two GPs thought their own advice to patients was all that was required: one had had training in psychiatry; the other thought that alcoholics came to no harm. One-third of the GPs were satisfied with the help available, and all of those used hospital facilities. The 36 doctors who were not satisfied almost all sought better hospital services for alcoholics, more special units, shorter waiting time and greater follow-up, including detoxification facilities. One-third asked for more social work services, including specially trained social workers. The remaining 'complaints' referred to the too ready availability of alcohol and to the lack of public health education about the dangers of excessive drinking.

TABLE V

Attitudes expressed towards alcoholics (numbers of responders in parentheses)	*Percentage agreeing*
Alcoholics are as deserving as other patients (53)	96
Rather an alcoholic registered elsewhere (52)	31
Easier to treat if there's some reason for it (51)	53
Waste of time to treat (53)	9
Waste of time to treat in GP (53)	28
Patient with gastritis—prefer if not alcoholic (52)	79
Homeless alcoholic should get priority over other homeless (49)	20
Female alcoholics worse to deal with than male (49)	45
When treating an alcoholic, would rather not be treating the family (51)	6
Alcoholics don't come to much harm (53)	9

Attitudes to alcoholics

Responses, in the form of agreement or disagreement with a number of attitudinal statements and beliefs, are shown in Table V; they reveal a considerable tolerance of alcoholics and sympathy with their plight. The overwhelming majority believed them to be as deserving of help as any other patients. Asked about the prognosis, four GPs (8%) told us that most patients got better; 35 (66%) said that few improved, and 14 (26%) believed that none did. Nine per cent thought that treating an alcoholic was a waste of time, although three times as many thought it could not usefully be done in a general practice setting. Age of doctor made no difference here, nor did it affect the 10% who thought that alcoholics did not come to much harm. Nearly half the GPs (including half the women doctors) found female alcoholics no harder to treat than male. Family support was considered important for treatment—hence the 94% who preferred it if they also treated the family; apparently, no conflict of interest was seen to arise. Whether a homeless alcoholic should have housing priority over other homeless people has moral overtones: should resources be devoted to the more needy or the more deserving? One-fifth of respondents thought that he should have priority. The high proportion preferring their patients' gastritis not to be due to alcoholism turned out only to be because alcoholic gastritis was viewed as more intractable.

Discussion

Sixty-two per cent of available GPs were interviewed; this response rate is at least as high as other studies in this subject. Over the telephone, the remainder seemed genuinely to be too busy; they did not seek to avoid the topic, but we have to presume that they were less interested. Except as indicated, neither the personal characteristics of the doctors nor the proximity of a specialist alcoholism unit correlated with specific views or courses of action.

There was no consensus about the definition of an alcoholic. A simple proposition that alcoholism may be diagnosed when two factors are present: frequent excessive drinking and resulting harm (social, psychological or physical, including dependence) could establish a useful congruence of viewpoint. If it is wished to retain the term 'problem drinker', it could be reserved for those who drink excessively but (so far) without harm.

The harms of alcoholism are protean, so we were expecting the variety of symptoms, signs and behaviours which alerted doctors, as well as the fact that they were so frequently told not by the patients but by others. Alcoholism was overwhelmingly seen as causing greater social than either medical or psychological problems. It is noteworthy, though, that one-third of the doctors sought confirmation of the diagnosis solely by asking about the amount consumed and not by questioning and examining to see what harms might be present; a history and examination are not complete unless that is done. Despite this, the GPs did not shirk attempting to make the diagnosis.

GPs retained a gloomier prognosis for alcoholics than is currently justifiable and this pessimism may inhibit efforts to persuade patients to accept treatment. Another factor was experience of the unwillingness of alcoholics to accept their problem and the frequency of relapse. GPs would value more help from alcoholism services, both medical and social. This perceived lack should be remedied because most doctors were willing to try and treat alcoholics, and they therefore deserve sufficient expert support. The specialist services cannot cope with the number of alcoholics requesting help unless they readily assist GPs in playing their part.

The younger doctors had all been taught about alcoholism in medical school; it is gratifying that so many had received postgraduate teaching as well. The differences in knowledge, and in some cases a degree of misinformation which we have disclosed, both point to the need for more teaching, particularly in the postgraduate setting. The advantage of authoritative material for private reading has been demonstrated.

The survey indicates the extent of GPs' understanding of alcoholism and of their capabilities. We must not infer that they always act as reported; nor, indeed, should they. Nevertheless, our findings reveal a considerably greater awareness and knowledge of the problems of alcoholism both medical and social, than was predictable from published statements. They also show a willingness, if not always to confront patients directly about their alcoholism, at any rate to tackle the medical and social consequences. It would not be a big step for them also to cope with the addiction itself. This is very encouraging, not least to providers of secondary services who may now know they can plan patients' treatment co-operatively with GPs working in primary care.

Acknowledgements

This study was undertaken during the elective period in AM's final student year. We gratefully acknowledge the help of those doctors who took part. Out of interest, the total cost of the study (stationery, stamps, telephone charges and bus fares) was under £55, met from the University Department's research fund.

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Alison Mowbray, MB, ChB

*Neil Kessel, MD, FRCP, FRCPsych, *Professor of Psychiatry*
University Department of Psychiatry, University Hospital of South Manchester, West Didsbury, Manchester M20 8LR.

*Correspondence

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Schizophrenia therapy: the importance of balance

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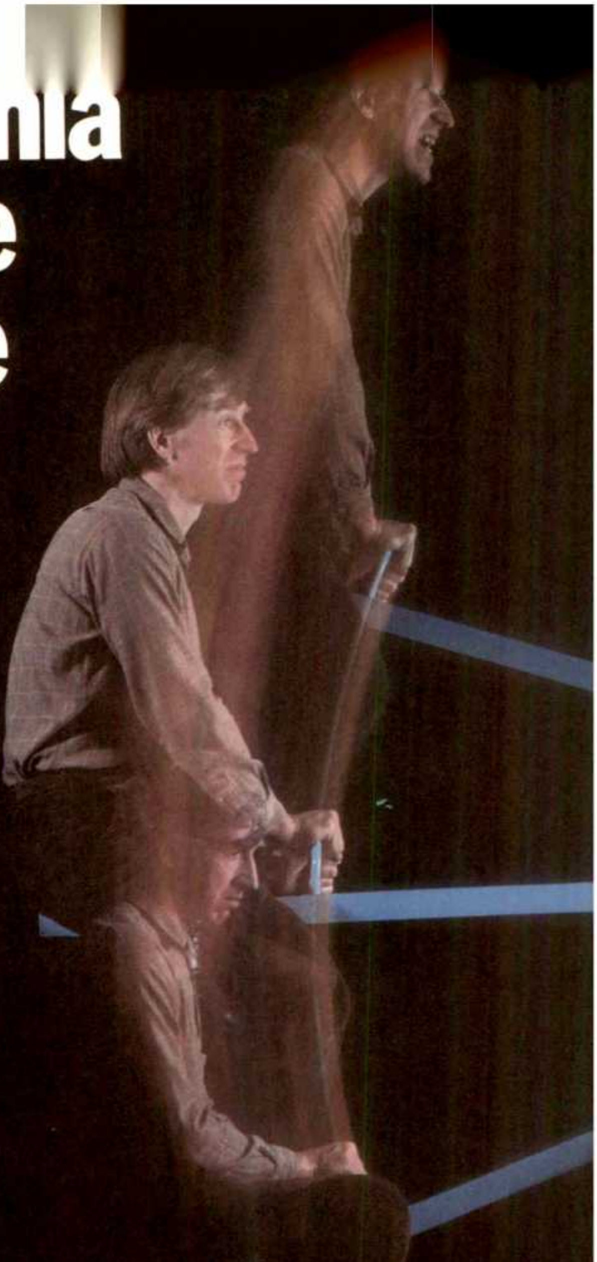

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Epilim may be given twice daily.
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t 600mg/daily increasing by 200mg
ay intervals until control is achieved
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t per day; in severe cases may be
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this only if plasma valproic acid
, clinical chemistry and haematological
eters can be monitored. **Combined
py** It may be necessary to raise the dose
used with anticonvulsants which induce
nzyme activity. Dosage of barbiturates
d be reduced if sedation is observed.
um dosage is mainly determined by
e control and routine measurement of
a levels is unnecessary. **Contra-
tions, Warnings; Contra-indication:**
liver disease. **Side effects:** Liver
nction including hepatic failure resulting
lities has occurred in patients whose
nent included valproic acid or sodium
ate. The incidents mainly occurred during
st 6 months of therapy. Clinical symptoms are
helpful than laboratory investigations
early stages of hepatic failure. The
of an acute illness, especially
the first 6 months, which may
e symptoms of vomiting,
gy or weakness, drowsiness,
xia, jaundice or loss of seizure
l is an indication for immediate
awal of the drug. Evidence to
oes not establish which
igation could predict this possible
se effect: measurement of liver
on should be performed in the
months of therapy in those who
most at risk. Hyperammonaemia
ut hepatic damage can occur, it is
y transient, but may occasionally
nt clinically. If so Epilim should be
ntinued. Valproic acid inhibits platelet
gation. Thrombocytopenia has been
ed. Spontaneous bruising or bleeding
ndication for withdrawal of medication.
eatitis, tremor, weight gain, transient
ss, increased alertness, aggressiveness,
activity, amenorrhoea, stupor and oedema
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se compounds should be weighed against the
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British Journal of Psychiatry (1986), **148**, 701–707

Does Propranolol have an Antipsychotic Effect?
A Placebo-Controlled Study in Acute Schizophrenia

RAHUL MANCHANDA and STEVEN R. HIRSCH

Thirty-six acute schizophrenics were randomly assigned to dextro (d)-propranolol or placebo in a double blind trial lasting four weeks. All patients had a fixed dose of haloperidol during the first week, which resulted in an initial improvement in both groups. Thereafter, a deterioration towards base-line was seen. Six patients on placebo, but none on propranolol were treatment failures at the end of three weeks ($P<0.001$). Comparison of change in scores from week 2 to 4 showed significantly greater deterioration in the placebo group; d-propranolol thus had a better effect than placebo in sustaining the initial improvement with haloperidol. The overall magnitude of clinical change from pre-treatment scores is small, the majority of the patients showing little or no overall improvement. It is concluded that d-propranolol has a detectable therapeutic effect, which by inference must have a novel pharmacological basis, but this is not as potent as standard neuroleptics.

The need to discover compounds which have potent antipsychotic effects but are different from conventional neuroleptics in their mode of action and associated side-effects continues. Of the several drugs investigated during the last decade, propranolol, a beta adrenoreceptor blocker, has received wide attention. The evidence in favour of an antipsychotic effect has ranged from empirical clinical observation (Atsmon & Blum, 1970) to uncontrolled trials (Atsmon *et al*, 1971; Yorkston *et al*, 1974; 1976; Sheppard, 1979, Hanssen *et al*, 1980) and more recent controlled studies. Of the controlled studies, some have supported such a claim (Yorkston *et al*, 1977; Lindstrom & Persson, 1980; Pugh *et al*, 1983), whereas others have failed to substantiate it (Myers *et al*, 1981; King *et al*, 1980; Peet *et al*, 1981a). The double-blind studies have, however, been conducted on chronic schizophrenics, and propranolol has been used as an adjunct to ongoing neuroleptic therapy in almost all the studies, apart from those by King *et al*, (1980) and Peet *et al* (1981a). The only controlled study carried out in acute schizophrenics compared propranolol with chlorpromazine (Yorkston *et al*, 1981), but did not have a placebo control.

The beneficial effects of propranolol in schizophrenia has been reported in its conventional racemic (d-1) form. Dextro (d)-propranolol, which is almost devoid of beta-adrenergic blocking activity (Shanks, 1976) and hence easier to use, was first investigated by us in an uncontrolled pilot study (Hirsch *et al*, 1981), and we reported that there was a definite improvement in seven out of nine schizophrenic patients. Interestingly, d-propranolol has no known effects on dopaminergic (Creese *et al*, 1978) or serotoninergic (Green & Graham-Smith, 1976) systems. Furthermore, psychological measures of habituation showed improvement with both (d-1) and d-propranolol consistent with the effect seen with conventional neuroleptics (Gruzelier *et al*, 1979). It was, therefore, thought that a double-blind placebo controlled study in acute schizophrenic patients would be directly relevant to the core question—does propranolol have antipsychotic activity?

Method

Sample

The sample consisted of recently admitted psychiatric inpatients suffering from acute or acute-on-chronic schizophrenia with florid delusions and/or hallucinations. The diagnosis of schizophrenia was arrived at independently by two psychiatrists and the patients were scrutinised by a structured interview, the Present State Examination (PSE) (Wing *et al*, 1974). Those patients who had received long acting neuroleptics in the last three weeks or oral medication in the last 10 days were not included. Patients with marked physical illness, in particular, any cardiorespiratory condition, organic cerebral disease, established history of alcoholism or drug abuse were excluded from the study. Detailed physical examination and investigations were carried out in every case. All patients and their nearest relative, where applicable, consented to participate in the study.

Treatment plan

After 3–7 days observation, patients were treated double blind for four weeks with identical capsules of d-propranolol or placebo (ICI Ltd). The trial medication was started with 40 mg qid with daily increments (except on weekends) of 160 mg. This increase was regulated by the patients' clinical state, response to treatment and his pulse and blood pressure before each dose. Pulse rate below 60/minute and/or blood pressure below 90/60 mm Hg necessiated missing that dose. All patients received haloperidol 5 mg bd with an anticholinergic, procyclidine 5 mg tds, during the first week of the trial only. This modification had to be made after a very poor recruitment of acute patients to the trial during the first eight months since neither d-propranolol nor placebo provided the sedation necessary to settle acute patients when first admitted. Also, a clinical judgement was made at the end of third week to decide whether a patient should go on to the fourth week based on improvement up to that time, and the urgency to ensure adequate treatment. If the patient was dropped from the study because of lack of improvement, end-point ratings were made at that time. After patients were discontinued or completed 3 or 4 weeks in the trial they were started on haloperidol 10–20 mgs per day for 4 weeks (in some cases higher doses) and reassessed 4 weeks later.

Assessment procedure

The psychiatric condition of the patients was evaluated by using the Brief Psychiatric Rating Scale (BPRS) (Overall & Gorham, 1962) and Manchester Scale (MS) (Krawiecka *et al*, 1977). These scales were administered at week 0, 1, 2 and 4 (or at the time of drop-out). On the BPRS the scores consisted of Total Score, Thought Disorder Score (sum of the scores of Conceptual disorganisation, Hallucinatory behaviour, Unusual thought content) and Non-Thought Disorder score (sum of Blunted affect, Emotional withdrawal, Suspiciousness, Grandiosity, Mannerisms or posturing, Hostility and Motor retardation). Thought disorder and Non-Thought Disorder scores together constitute the Schizophrenia Score. The rest of the items on the BPRS constitute the Non-Schizophrenia Score. The scores on the MS consisted of Total Score, Positive Score (sum of Delusions, Hallucinations and Thought disorder and Incongruity of affect), Negative Score (sum of Poverty of speech, Blunted affect) and Non-specific Score (sum of Anxiety, Depression and Motor retardation). In addition patients were rated pre and post trial by a Nurses Rating Scale used by us in a previous study (Manchanda & Hirsch, 1981). A change in the global severity of illness (worse, unchanged, mild, moderate, marked improvement, and recovered) was recorded at the end of the trial and after four weeks on conventional neuroleptic (haloperidol) given post trial.

Results

Forty-six newly admitted patients with an acute or acute on chronic episode of schizophrenia consented to participate in the trial during a period of 30 months; ten patients, however, refused medication during the first week, and therefore were not entered into the trial. Random allocation resulted in an equal number of patients in the d-propranolol ($n = 18$) and placebo group ($n = 18$). Patients' socio-demographic and clinical characteristics are shown in Table I. There was no statistical difference between the two groups on any measure. Also, there was no difference (using Mann Whitney Test) between the d-propranolol and placebo groups in the pretreatment total scores and subscores on the BPRS and MS.

Although no patient had received long-acting depot neuroleptics within three weeks of starting the trial, one patient in the propranolol group and five in the placebo group had been on long-acting neuroleptics in the previous year to starting the trial. The patient in the propranolol group had the last injection (fluphenazine decanoate 25 mgm) 6 weeks before entering the trial. Of the patients in the placebo group, 3 had discontinued it 10–12 months before entering the trial. The remaining two had received their injections (fluphenazine decanoate 12.5 mgm and depixol 40 mgm) 6 weeks previously. Thus, the difference in depot medication preceding the trial is only one patient in the placebo group receiving 12.5 mgm of fluphenazine decanoate, and this would tend to bias the results against propranolol.

The maximum dose in the d-propranolol group ranged between 800–1760 mg/day mean 14010 mg/day) and in the placebo group the number of capsules prescribed was comparable to 1120–2080 mg/day (mean 1562 mg/day) of propranolol. The number of days taken to reach the maximum dose was 15.5 and 17 respectively. Six patients on placebo, compared to none in the propranolol group, were treatment failures at the end of three weeks ($P < 0.001$), and two patients (one in each group) were dropped out at 2½ weeks as they became suicidal. Figs. 1 and 2 show the change in mean Total score (week by week) on the BPRS and on the MS. Figs. 3 and 4 show the change in mean subscores on these two scales.

Not unexpectedly, the scores in both groups (Figs. 1–4) reduced markedly by the end of one week, as all patients received haloperidol. Also, there was a significant reduction between pre- and post-treatment scores in the propranolol group on The Thought Disorder ($P = 0.01$), Schizophrenia ($P = 0.01$) and Total ($P = 0.02$) Scores of the BPRS as well as on the Positive ($P = 0.03$) and Non-Scientific ($P = 0.04$) score of the Manchester Scale (MS). However, a between-group comparison of the change in scores at the end of the trial (week 0 minus week 4 rating for each group, including drop-outs at week 3) showed that the propranolol group was not significantly different from the placebo group (using Mann Whitney/Wilcoxon Rank Sum Test) in measures of Total score as well as various sub-scores on the BPRS and the MS. The change in score for each item on the BPRS ($n = 19$) and MS ($n = 9$) was also calculated. Only one item (Blunted Affect) on both scales distinguishes the two groups, those on d-propranolol significantly better than placebo ($P < 0.05$).

The percentage change in Total and Schizophrenia subscore of BPRS and MS showed that majority of the patients in both d-propranolol (10/18) and placebo group (13/18)

TABLE I
Socio demographic and clinical variables in trial groups

	d-Propranolol (n=18)	*Placebo (n=18)*
Sex M	10	8
Age (mean and range)	32.3 (18–55)	33.2 (20–58)
Age at onset (Mean and range)	27 (18–45)	28 (16–56)
No. of previous admissions		
Nil	7	3
1–4	10	14
NK	1	1
Episodes treated (Mean and range)	2.6 (1–5)	3 (1–7)
Most recent illness		
No previous episode	6	2
Within 6 months	10	14
6–12 months	2	2
Catego subclasses		
Nuclear schizophrenia	7	7
Catatonic schizophrenia	2	5
Paranoid psychoses	3	3
Affective psychoses	3	1
Schizophrenia without FRS	2	2
Borderline psychoses	1	—

None of the differences between the scores in each group were statistically significant.

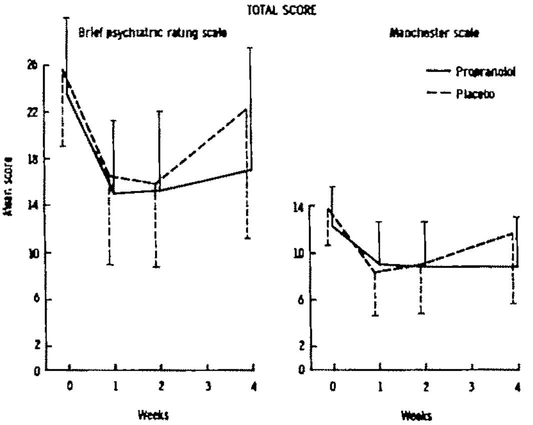

FIG. 1. The mean changes in total scores in the propranolol and placebo groups on the BPRS and MS over 4 weeks are shown. The vertical line equals one standard deviation. There was a significant difference in the Total Score in the propranolol group as measured on the BPRS [23.3 [wk. 0] vs 17.1 [wk. 4], $P=0.02$] but not on the MS [12.2 & 8.8 respectively]. The findings on the BPRS was not significant when compared with the placebo group [25.6 [wk. 0], 22.2 [wk. 4]]. Between wk. 2 to 4, significantly greater deterioration [$P<0.05$] was seen in the placebo [wk. 2 mean score = 15.9 [BPRS], 9.1 [MS]] as compared to the propranolol group [wk. 2 mean score = 15.2 [BPRS], 8.9 [MS]]

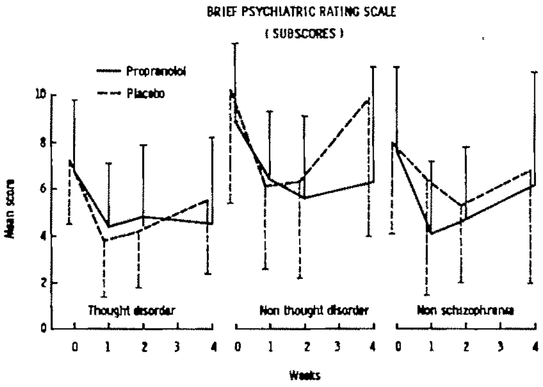

FIG. 2. The mean changes in BPRS sub-scores are shown. A significant reduction [$P=0.01$] was seen in the propranolol group on Thought Disorder subscore [6.8 [wk. 0] vs 4.5 [wk. 4]], but the finding was not significant when compared to the placebo group [7.2 [wk. 0], 5.5 [wk. 4]]. Between week 2 and 4 the improvement was maintained on Thought Disorder subscore and there was less deterioration on Non-Thought Disorder sub-score in the propranolol group, compared to placebo group [$P<0.05$]. There was no difference in the Non-Schizophrenia sub-score.

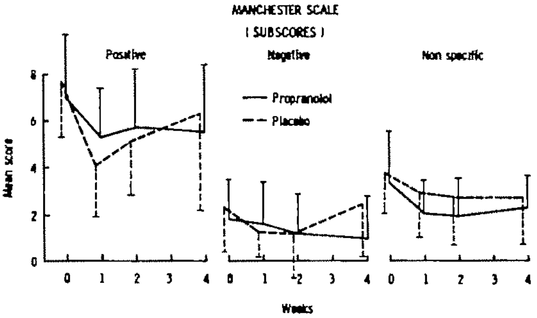

FIG. 3 Shows the change in mean subscore on the MS. There was a significant reduction [$P < 0.05$] in the Positive [7.0 [wk. 0] vs. 5.5 [wk. 4]] and non specific subscores [3.3 [wk. 0] vs. 1.9 [wk. 4]] in the propranolol group but the finding is not significant when compared to the placebo group. Between week 2 and 4 there is a significant difference [$P < 0.05$] between propranolol and placebo groups in the Positive and Negative subscores but not in the Non Specific subscore.

showed less than 25% improvement at the end of the trial (see Tables II & III). Comparisons of these findings for d-propranolol and placebo group were not significant using the chi square test. There was no significant change in either group in the Nurses' rating carried out before and at the end of the trial. None of the patients in the d-propranolol group had a major side-effect or hypotension necessitating discontinuation of the trial. Side-effects when reported (in both groups) were minor, and did not require any intervention.

Indication of anti-psychotic effect

There were, however, some novel findings, Firstly, seven patients in the placebo group, compared to only one in the propranolol group, could not complete the 4-week trial. Secondly, although the overall clinical effect is small, discontinuing haloperidol after one week was followed by significantly greater deterioration in the placebo group, as compared to the propranolol group (Figs. 1–4), suggesting a pharmacological effect for propranolol. A comparison between the two groups of the change in scores from the end of week 2 (one week after discontinuing haloperidol) to the end of the trial showed significant difference on the sub-scores of Thought Disorder ($P = 0.04$), Non-Thought Disorder ($P = 0.04$) and Total score ($P = 0.03$) of the BPRS as well as on the Positive ($P = 0.04$), Negative ($P = 0.04$) and Total score of the MS ($P = 0.02$) but the findings were not significant for the Non-Schizophrenia score ($P = 0.66$) of BPRS and Non-Specific score of MS ($P = 0.54$). Thus, there appears to be a specific effect on schizophrenic symptomatology. The finding that the overall clinical effect is small is further supported by Table IV. It shows that on a global scale, majority of the patients in both

TABLE II
Percentage change in total score

	<25%		*25–50%*		*51–75%*		*>75%*	
	BPRS	*MS*	*BPRS*	*MS*	*BPRS*	*MS*	*BPRS*	*MS*
Propranolol (*n* = 18)	10	9	3	7	2	1	3	1
Placebo (*n* = 18)	13	10	2	5	2	2	1	1

$x^2 = 1.5913$ DF = 3 NS
$x^2 = 0.719298$ DF = 3 NS

TABLE III
Percentage change in schizophrenia score

	<25%		*25–50%*		*51–75%*		*>75%*	
	BPRS	*MS*	*BPRS*	*MS*	*BPRS*	*MS*	*BPRS*	*MS*
Propranolol (*n* = 18)	9	9	1	6	5	1	3	2
Placebo (*n* = 18)	11	10	3	5	2	3	2	—

$x^2 = 2.68571$ DF = 3 NS
$x^2 = 3.14354$ DF = 3 NS
In both tables the percentage change in Total Score and Schizophrenia Score on The Brief Psychiatric Rating Scale (BPRS) and Manchester Scale (MS) are shown. Percent change in score = Baseline Score − Final Score/Baseline Score × 100 Schizophrenia score on the BPRS is the sum of Thought Disorder and Non Thought Disorder Subscores and on the MS it is the sum of Positive and Negative subscores. The end point score of 6 patients on placebo who were treatment failures at 3 weeks, and 2 (one in each group) who were dropped out at $2\frac{1}{2}$ weeks because they were suicidal are included.

TABLE IV
Global change

	Propranolol (*end of trial*)	*Placebo* (*end of trial*)	*Haloperidol* (*4 wks. post trial*)
Completely remitted	2	2	4
Marked improvement	1	0	8
Moderate improvement	3	2	17
Mild improvement	1	2	4
Unchanged	8	6	2
Worsened	3	6	0
	18	18	35

$x^2 = 22.1955$ DF$=2$ $P<0.001$
(Mod.—complete rem. vs Mild-unchanged)
One patient was lost in the follow-up.

groups were unchanged or deteriorated (11 of 18 on d-propranolol and 12 of 18 on placebo) by the end of the trial. The group as a whole was treatment-responsive, as suggested by the improvement in both groups during the initial one week of treatment with haloperidol. Further, open treatment with haloperidol from weeks 5–8 resulted in moderate or better improvement in 29 out of 35 patients, as compared to the propranolol and placebo groups, wherein only six and four patients respectively showed a similar global improvement ($P<0.001$), see Table IV).

Discussion

This is the first placebo-controlled trial to evaluate the efficacy of propranolol in acute schizophrenia. Given the inconsistency between several research findings which found that propranolol has an antipsychotic effect and others which failed to find an effect, we had set out to answer the fundamental question of whether or not propranolol has an antipsychotic action. The two groups matched on sociodemographic variables, clinical characteristics, and pretreatment scores, and eventually proved responsive to a conventional neuroleptic, haloperidol.

In terms of clinical efficacy, this study failed to show an appreciable effect for d-propranolol in the treatment of acute schizophrenia. The majority of the patients in both groups showed less than 25% improvement on Schizophrenia score of the BPRS and the MS. Also, a large number of patients on d-propranolol ($n=11$) or placebo ($n=12$) were globally unchanged or worse at the end of the trial and two patients in each group had remitted. A between-group comparison found that the change in scores of the propranolol group was not significantly different from the placebo group over the trial period. This result is consistent with the only other controlled study on acute schizophrenics, that of Yorkston *et al.* (1981), who were unable to find a significant overall difference between propranolol and chlorpromazine. Like our study, no significant difference was found between the two groups in either the Thought Disorder or Non-Thought disorder sub-score of the BPRS. Although there wasn't a placebo group, it is noteworthy that the mean peak dose of chlorpromazine was only 300 mg. At this dose, chlorpromazine has not been found to be better than placebo in 9 out of 26 trials (Davis & Garver, 1978). Also, when the change in score of individual items was considered, Yorkston *et al* found significantly less reduction in conceptual disorganisation for patients treated with propranolol. The effect of propranolol was modest, and half of the patients on propranolol showed minimal or no improvement.

The present study, however, showed a significant pharmacological effect of d-propranolol, when compared to placebo: d-Propranolol had a small but discernable effect in sustaining the improvement obtained from one week of treatment with haloperidol. Statistically, there was a difference between the d-propranolol and placebo groups on the change in scores between week 2 and 4, the placebo group having deteriorated significantly more on various sub-scores of the BPRS and the MS (Figs. 1–4, see Results). Both positive and negative symptom scores deteriorated more on placebo than propranolol. What is the explanation for such an effect? Is it possible that d-propranolol sustained or stabilised the beneficial effect of haloperidol observed during the first week of combined treatment? Peet *et al* (1981b) showed that there is a pharmacokinetic interaction between chlorpromazine and propranolol, resulting

TABLE V
Plasma haloperidol levels

	Week 2	*Week 4*
D-Propranolol	0.49* ($n=6$)	0.16 ($n=6$)
Placebo	0.23 ($n=9$)	0.10 ($n=4$)

Table V shows the mean plasma haloperidol levels (estimated by extracted haloperidol radioimmuno assay) for a subsample of trial patients. *Comparatively higher value because of 1 patient. The mean taking out this extreme value was 0.24 ng/ml.

in higher levels of chlorpromazine sulfoxide in patients receiving a combined treatment, but there is no evidence to generalise the statement to include other neuroleptics such as haloperidol. In any case, a sub-group of patients in this trial had haloperidol assays, but the levels in both groups at week 2 (<0.5 ng/ml) and at week 4 (<0.16 ng/ml) were far below the expected therapeutic levels of haloperidol (>5.0 ng/ml) and therefore of no clinical significance (Table V).

Some double-blind placebo-controlled studies on chronic patients have failed to find any advantage for propranolol over placebo (Peet *et al*, 1981a; King *et al*, 1980). However, a recent controlled study by Puch *et al* (1983) showed that propranolol was more effective than placebo. Although this study was in chronic schizophrenics on concommitant neuroleptics, all patients had florid symptoms as an inclusion criterion. The observed change was, however, not so great as reported in earlier uncontrolled studies. Improvement was observed on the 'irritability' sub-score of a nurses' rating scale, the NOSIE (Honigfeld & Klett, 1965). The change on schizophrenia sub-score of the Comprehensive Psychopathological Rating Scale (CPRS) (Asberg *et al*, 1978) just reached a significance level ($P=0.046$) and that at the end of 8 weeks. No significant change was observed on the BPRS. We have argued elsewhere (Manchanda and Hirsch, 1984) that the schizophrenia scale of CPRS has a bias in including only those items which are sensitive to change over time and not necessarily with treatment alone. Further, given the large number of analyses attempted, the observed level of significance in the absence of other significant results cannot be regarded as a definitive finding for a clinical effect of propranolol in the treatment of schizophrenia.

The present double-blind study was initiated because of the encouraging preliminary results with d-propranolol and the ease in using it on account of minimal beta-blocking activity. However, could it be that the racemic (d-l) propranolol and not the dextro(d)-propranolol has a clinical antipsychotic effect? Moller *et al* (1979) used (d) and (d-l) propranolol in six manic patients, and found that an anti-manic action is exerted by both preparations of propranolol. Based on this study and findings from a previous study (Emrich *et al*, 1979), they concluded that the anti-manic effect of d-propranolol (dose range 2000–3000 mg/day) is on average about half that of (d-l) propranolol. Although the dose of d-propranolol used in the present study (800–1760 mg/day) is lower than the above study, studies using 400–900 mg of (d-l) isomer have also reported a positive effect (Yorkston *et al*, 1974), 1977, Pugh *et al*, 1983). Thus, the lack of a clinical antipyschotic effect is observed, despite using adequate dosage in the present study.

This trial highlights once again the need for double-blind studies to confirm the positive effects observed in an uncontrolled study such as ours (Hirsch *et al*, 1981). Alternatively, it is recommended that the criteria for measuring change in uncontrolled studies should be stricter, such that improvement should be based on at least 75% change in score. Re-analysis of our uncontrolled study on these criteria results in an improvement in two or at the most three out of nine patients. This result is more consistent with the findings on the present controlled study.

In conclusion, it appears that d-propranolol has a pharmacological effect on schizophrenic symptomatology which is evident on rating scales, but this effect does not compare favourably with conventional neuroleptics as a clinical agent. Of particular interest is the effect seen in the negative symptoms of schizophrenia—symptoms which generally do not respond to currently available neuroleptics. The findings in this study should be of interest to neuropharmacologists because they point to the possibility that d-propranolol, a non-neuroleptic agent with no known effects on the beta-adrenergic, dopaminergic or serotoninergic system, has a specific pharmacological effect on the positive as well as negative symptoms of schizophrenia which is not associated with an improvement in the non-specific symptoms. Whether or not propranolol can be modified to produce a more effective anti-psychotic effect provides a challenge to the pharmaceutical industry which we hope will be taken up.

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Rahul Manchanda, MBBS, MD, MRC Psych, *Formerly Lecturer in the Academic Department of Psychiatry at Charing Cross & Westminster Medical School. Currently Assistant Professor of Psychiatry, University of Western Ontario and Director of Education, St. Thomas Psychiatric Hospital, P.O. Box 2004, St. Thomas, Ontario, Canada, 1ND5 3V9.*

*Steven R. Hirsch, BA, MD, MPhil, FRCP, FRC Psych, *Professor of Psychiatry, Charing Cross Hospital Medical School, Fulham Palace Road, London, W6 8RF.*

*Correspondence.

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Ethnic Differences in Self-poisoning: A Comparison of Asian and White Groups

JOHN MERRILL AND JOHN OWENS

The characteristics of Asian patients admitted to a Birmingham hospital following deliberate self-poisoning were compared with those of British-born white self-poisoners. Asian patients were more likely to be young, female, and married. They were less likely to have previously self-poisoned, received previous psychiatric treatment, be diagnosed psychiatrically ill, or suffer from a personality disorder. Culture conflict was common among the Asian patients and was present in the majority of unmarried Asian females. The rate of self-poisoning for Asian females was higher than for white females, but for Asian males was lower than for white males.

Those responsible for the management of people who 'overdose' or poison themselves are helped in their task by a vast array of literature (e.g. Kreitman, 1977; Morgan, 1979; Hawton & Catalan, 1982). All aspects of this behaviour have been extensively studied except one—the ethnic group of the person. The few studies that have investigated self-poisoning and ethnicity have found marked differences between Asian, Irish, West Indian, and White groups.

Burke retrospectively studied case notes of Asian, Irish, and West Indian patients admitted to Birmingham hospitals after attempting suicide between 1969 and 1972 (Burke, 1976a, b and c). He found that the Asian patients were under-represented and that they were young, rarely abused drugs or alcohol, and rarely repeated the attempt.

A pilot study from this centre (Wright *et al*, 1981) found that Asian self-poisoners were more likely to be young, married, and female than were White self-poisoners. "Transcultural" problems were common, and the mean annual rate of increase in self-poisoning between 1975 and 1979 was higher for Asians than Whites.

This study compares demographic, social, and psychiatric characteristics of Asian and White self-poisoners respectively, and estimates the rate of self-poisoning in each group.

Method

Patients The study was carried out between January 1st 1979 and December 31st 1981 on all patients admitted following deliberate self-poisoning to Dudley Road Hospital, Birmingham. The hospital serves a catchment area of 194,270, 22.33% of whom were born outside the UK, 10.8% being born in India, Pakistan, or Bangladesh. Patients attending the casualty department after deliberately taking more than the prescribed amount of a medical substance or after taking substances not intended for human consumption were routinely admitted to the West Midlands Poisons Unit, pending psychiatric assessment. A small proportion (estimated at under 5%) refused admission, and were not included in the study. When patients were admitted on more than one occasion during the three years of the study, details of their first admission only were included.

Data on patients from two ethnic groups, White and Asian, were compared. The 975 White patients consisted of all whites born in England, Scotland and Wales. Patients born in Northern or Southern Ireland were excluded because of Burke's finding that among attempted suicides in Birmingham, the Irish-born were over-represented (Burke 1976b). The 196 Asian patients consisted of 139 (70.9%) born in India, Pakistan, or Bangladesh, 52 (26.5%) of Asian origin born in the United Kingdom and five (2.6%) of Asian origin born in East Africa. Patients of mixed ethnic origin were excluded from the study.

Assessment Assessment of patients was performed by one author (JO) or a member of his team, soon after admission. A coding sheet detailing items of social, psychiatric, and medical interest was completed on every patient; nursing, medical, and psychiatric staff each completed appropriate sections. Most of the Asians spoke good English, so that an interpreter was seldom used. Whilst much of the data recorded in the results is self-explanatory, some items require further clarification. "Marital Problems" were recorded if at interview, the patient indicated that difficulties in the marriage were at least part of the reason for self-poisoning. "Culture Conflict" was serious difficulty, due either to conflict over traditional customs or racial prejudice, which was seen by the patient as being at least part of the reason for self-poisoning. Patients were asked if they had previously self-poisoned (whether resulting in hospital admission or not) and if they had previously received psychiatric treatment (as an outpatient or inpatient). The diagnosis of alcoholism, psychiatric illness, or personality disorder was made by the assessment psychiatrist.

Comparisons Data on the two ethnic groups were compared by means of the Chi-squared test using Yates' correction for all items except the age distribution for which the Mann-Whitney U test was used.

Direct comparisons would only be valid if the groups were of similar social class (Buglass, 1976) and age-structure (Kreitman, 1976). The social class of the groups was similar, 87.8% of White and 88.6% of the Asian patients being classes IV and V, according to the Registrar General's classification (OPCS, 1970). The age-structure, however, differed greatly, there being very few older Asian patients. A separate comparison of patients aged under 35 with those over 35 revealed statistically significant differences for three items (previously psychiatric treatment, psychiatric diagnosis, and psychiatric follow-up). These age-dependent items therefore were compared only for patients aged under 35, comparison of the older age-group being precluded due to the small number of older Asians.

In some of the results given, the total number is less than the number of patients falling into that group. This is because some items of information were not available on all patients.

Calculation of rates Overall rates were calculated for patients born in England, Scotland, and Wales (UK-born) and India, Pakistan, and Bangladesh (Asian-born), using the Small Area Statistics for the catchment area (OPCS, 1981b). Age-specific rates were calculated by extrapolating from the age-group/country of birth analyses for the West Midlands Metropolitan County (OPCS, 1981a).

Results

See Table I.

Sex, age and civil status

The female:male ratio of 2.9 for Asians was significantly greater than that of 1.5 for the White group. The age-distribution of both male and female Asians was much younger than that of the White group, which was due to a lack of older Asian patients and to the modal age-group for Asian males being younger than for White males. Compared to White patients both Asian males and females were significantly more often married; Asian females were significantly less often 'divorced and separated' or widowed.

Marital problems and culture conflict

Although marital problems were reported less by Asian than by White males, the difference was not significant. Asian females, however, reported marital problems significantly more often than White females, and many of these problems were due to culture conflict. Fourteen Asian females blamed their marital problems on arranged marriages that were never wanted, four of their husbands demanding they behave in a less westernised fashion, and three on their mothers-in-law interfering with the way they ran their lives and marriages.

Of the unmarried patients, five White females had relationships with coloured boyfriends of which their parents disapproved, one Asian male rejected his imminent arranged marriage, and one complained of parental disapproval of his westernised lifestyle. Thirty-one Asian females rejected proposed arranged marriages and/or rebelled against their parents imposing what they saw as restrictive Asian customs (e.g. not allowing them to go out at night, mix with boys, or take further education). Three Asian females said they were victims of racialist bullying at school.

Alcoholism

The incidence of alcoholism in Asian and White males was similar. No Asian females had alcoholism diagnosed.

Previous self-poisoning and previous psychiatric treatment

Significantly fewer Asian males and females than Whites had previously self-poisoned. Asian females aged under 35 years were significantly less likely to have received previous psychiatric treatment.

Psychiatric diagnosis

Significantly fewer Asian females aged under 35 years were diagnosed as suffering from a psychiatric illness. No significant difference was found between the groups for any of the diagnostic categories. Personality disorder was diagnosed in significantly fewer Asian than White patients.

Follow-up

There was no significant difference between groups for the type of psychiatric follow-up offered, though significantly more Asian females were followed-up by the psychiatric social worker attached to the unit.

Others

Other items looked into but not recorded in Table I included the proportion of females pregnant, the incidence of self-poisoning and suicide in relatives and friends of the patient, accumulation of debts, a history of violence by and against the patient in the previous year, living in overcrowded conditions, and separation from mother and father before the age of ten. None of these revealed significant differences between the groups.

Rate of self-poisoning

The annual rates of self-poisoning for males and females are shown in Tables II and III respectively. Rates for Asian-born males were significantly lower than for UK-born males in age-groups over 25 years and overall.

TABLE I

Characteristics of self-poisoning compared by ethnic group

	White		*Asian*		*Significance (White vs. Asian)*	
	Male	*Female*	*Male*	*Female*	*Male*	*Female*
Age group						
(*n*)	(383)	(592)	(50)	(146)		
<35 yrs (%)	66.8	66.4	82.0	92.5		
35–54 yrs (%)	24.0	22.5	18.1	4.1	$P<0.01$	$P<0.0001$
<55 yrs (%)	9.1	11.2	0.0	3.4		
Mean Age (yrs)	32.0	31.3	26.7	23.1		
Modal Age-Group (yrs)	25–29	15–19	20–24	15–19		
Civil status						
(*n*)	(364)	(575)	(49)	(145)		
Married (%)	33.8	32.3	53.1	56.6	$P<0.025$	$P<0.0005$
Single (%)	50.6	47.3	36.7	38.6	NS	NS
Divorced + Separated (%)	12.4	12.3	6.1	2.8	NS	$P<0.005$
Widowed (%)	3.3	8.0	4.1	2.1	NS	$P<0.025$
Marital problems						
(Number married)	(145)	(226)	(26)	(85)		
Marital problems (%)	48.3	49.1	38.5	71.8	NS	$P<0.001$
Culture conflict						
(Number single)	(184)	(272)	(18)	(56)		
Cultural problems (%)	0.0	1.8	11.1	60.7	$P<0.001$	$P<0.0005$
Alcoholism						
(*n*)	(378)	(588)	(49)	(145)		
Alcoholism (%)	9.8	4.6	14.3	0.0	NS	$P<0.025$
Previous self-poisoning						
(*n*)	(382)	(591)	(50)	(146)		
Previous self-poisoning (%)	33.2	34.0	14.0	21.9	$P<0.01$	$P<0.01$
Previous psychiatric treatment						
(*n* aged <35 yrs)	(255)	(393)	(41)	(135)		
Previous psychiatric treatment (%)	30.5	20.1	14.6	11.1	NS	$P<0.05$
Psychiatric diagnosis						
(*n* aged <35 yrs)	(253)	(392)	(41)	(135)		
No psychiatric illness (%)	76.7	70.7	80.5	82.2	NS	$P<0.025$
Depressive illness (%)	4.0	5.9	4.9	5.2	NS	NS
Reactive depression (%)	6.7	15.3	7.3	8.9	NS	NS
Organic psychiatric disorder (%)	4.7	1.5	2.4	0.7	NS	NS
Schizophrenia (%)	5.5	2.0	4.9	1.5	NS	NS
Other (%)	2.4	4.6	0.0	1.5	NS	NS
Personality disorder						
(*n*)	(378)	(588)	(49)	(145)		
Personality disorder (%)	25.7	22.1	8.2	7.6	$P<0.025$	$P<0.0005$
Psychiatric follow-up						
(*n* aged <35 yrs)	(251)	(389)	(41)	(135)		
No psychiatric follow-up (%)	63.3	69.4	68.3	77.8	NS	NS
In patient (%)	5.6	4.4	9.8	0.7	NS	NS
Day patient (%)	2.0	1.5	2.4	0.7	NS	NS
Out patient (%)	29.1	24.7	19.3	20.7	NS	NS
Social work follow-up						
(*n*)	(380)	(590)	(50)	(146)		
Social work follow-up (%)	3.7	12.4	8.0	24.7	NS	$P<0.0005$

TABLE II

Male rates of self-poisoning (per 100,000 per year) compared by ethnic group

Age-Group	*Population*		*Patients*		*Rate (per 100,000 per year)*		
	UK-born	*Asian-born*	*UK-born*	*Asian-born*	*UK-born*	*Asian-born*	*Significance*
<15 yrs	19,154	1,462	25	1	44	23	NS
16–24 yrs	11,057	2,002	130	15	392	250	NS
25–34 yrs	9,580	2,967	126	13	438	146	$P<0.0005$
35–44 yrs	8,329	2,072	60	5	240	80	$P<0.025$
>45 yrs	24,238	3,532	71	3	98	28	$P<0.05$
Overall	72,358	12,036	412	37	190	102	$P<0.0005$

TABLE III

Female rates of self-poisoning (per 100,000 per year) compared by ethnic group

Age-Group	*Population*		*Patients*		*Rate (per 100,000 per year)*		
	UK-born	*Asian-born*	*UK-born*	*Asian-born*	*UK-born*	*Asian-born*	*Significance*
<15 yrs	18,417	910	86	4	156	146	NS
16–24 yrs	10,825	1,802	280	49	862	906	NS
25–34 yrs	9,348	2,594	125	39	446	501	NS
35–44 yrs	8,282	1,648	79	4	318	81	NS
>45 yrs	30,153	2,074	120	6	133	96	NS
Overall	77,025	9,028	690	102	299	376	$P<0.05$

The overall rate for Asian-born females was significantly higher than that for UK-born females, but there was no significant difference for age-specific rates.

Discussion

It is important to consider the validity of the information obtained: some items (e.g. sex, age, marital status, follow-up) are highly reliable, whereas others (e.g. cultural and marital problems, previous self-poisoning, past psychiatric treatment) are dependent on the information supplied by the patient. The diagnosis of alcoholism, psychiatric illness, and personality disorder depends both on information supplied by the patient and on the assessor's interpretation of it. All the assessors were white, and it could be postulated that they would have had difficulty diagnosing psychiatric disorder in Asian patients.

The calculated rate of self-poisoning is subject to inaccuracies. An unknown number of patients included in the study came from outside the hospital's catchment area, and no doubt many cases of self-poisoning from within the catchment area attended other hospitals. Census data contain information on country of birth and not on ethnic group, so that some non-white patients (e.g. British-born Asians and West Indians) had to be included in the calculations of UK-born rates. Many cases, of course, will not have presented at hospital at all.

The Asian group is heterogeneous, including patients of different country of birth and different religion: in this study, most Asians (59.7%) were Indian Sikhs. A separate analysis comparing characteristics of Asian sub-groups, although involving small numbers, revealed only one difference—six out of the seven Asian males with alcoholism were Sikh. It seems that alcoholism in the male Sikh community is a rapidly escalating problem, as indicated by increasing numbers presenting at specialist centres (Kahn, 1984).

The relative excess of marital problems in Asian females, compared with White females, could be seen as being due to those patients who blamed their marital problems on unwanted arranged marriages. However, marriages go wrong for many reasons, and if the marriage was arranged, there is likely to be a strong tendency to blame the 'arrangement' and ignore other factors. There was also a marked difference between the proportion of Asian males and Asian females with marital problems, while no Asian males blamed their marital problems on unwanted arrangements: this may have been due to the practice of Asian wives coming to Britain to join their husbands or Asian women coming here to get married. When this happens, the woman has to face the stresses of immigration without the support of her own family.

Overt racial prejudice, although rife in the community, was implicated in only three Asian self-poisonings: this may have been due to under-reporting to a white psychiatrist. Alternatively, racism may have been involved indirectly in the genesis of depression (Fernando, 1984). Culture conflict affecting other Asian patients centred around family discord over Asian versus western lifestyles: the patients affected were predominantly unmarried adolescent girls, who saw their problems as being insoluble. The choice they had was between being ostracised from their families and the supportive Asian community or abandoning their desire for a less restrictive lifestyle. In reality, the dichotomy was seldom so clear-cut, and a compromise could usually be found. Many of these patients were helped by the unit's social worker, who was experienced in working with Asian families. More recently, the local Asian Resource Centre has provided valuable assistance, sometimes by taking the women into their hostel for a 'cooling off' period. Similar culture conflict was found in eight out of 25 Indian males and in 46 out of 75 Indian females attempting suicide in South Africa by Cheetham *et al* (1983).

In Pakistan and India, attempted suicide is predominately a male activity and incidence rates are low, ranging from 0.72 per 100,000 per year in Karachi (Ahmed & Zuberi, 1981) to 43 per 100,000 per year in Madurai (Rao, 1965). Burke (1976a) found that the rate of attempted suicide amongst Asians aged 15–64 in Birmingham between 1969 and 1972 was 57 and 126 per 100,000 per year for males and females respectively. Wright *et al* (1981) found the annual rate of increase in self-poisoning between 1976 and 1979 to be higher for Asians than Whites. The evidence from this study suggests that for Asian females, the rate may now be higher than for White females, and that culture conflict is frequently implicated.

It is important that those responsible for the management of Asian self-poisoners are aware of the frequency of the problem and of the factors involved. If a person self-poisons as a 'cry for help' (Stengel & Cook, 1958), 'to get relief from a terrible state of mind', or to 'escape for a while from an impossible situation' (Bancroft *et al,* 1979), a knowledge of the problems of Asian self-poisoners may help in the understanding of difficulties facing Asians living in Britain.

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*John Merrill, MB, ChB, MRCPsych, *Senior Registrar, All Saints Hospital, Lodge Road, Winson Green, Birmingham, B18 5SD.*

John Owens, MB, ChB, MRCPsych, *Consultant Psychiatrist, All Saints Hospital and Regional Poisons Unit, Dudley Road Hospital; Senior Clinical Lecturer, University of Birmingham.*

*Correspondence

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Comment

Causal Models in Psychiatric Research

MATTHEW J. EDLUND

The nature of causal explanation remains a conceptual difficulty for psychiatric research. Most research workers and clinicians can describe their processes of causal inference with reference to some empirical example close at hand. Yet such demonstrations are themselves based on more fundamental abstract models that are themselves left unstated. Psychiatric classificatory schemata presently used in research possess unwritten, underlying assumptions regarding causality, and these assumptions need examination.

At present, DSM-III is the most prominent American psychiatric classificatory system, ICD-9 the most prominent British classification (American Psychiatric Association, 1980; World Health Organization, 1978). Following the lead of the Research Diagnostic Criteria, DSM-III is designed to bridge the varied schools of causality present in the United States, and devise a 'clinically useful', 'atheoretical' document that can be of use to everyone. Despite its avowedly atheoretical approach, DSM-III does, in fact, operate with a distinct idea of how causality occurs, through the notion of exclusionary criteria. By virtue of its hierarchical scheme (Foulds, 1976), one disease is said to be 'due to' another, even though there is often little or no empirical basis for such a judgement. A recent paper by Boyd *et al* (1984) describes not only this hidden causality inherent in DSM-III, but also how the products of such causal thinking, given present circumstances, are suspect. Panic disorder is not panic disorder if it is 'caused' by somatization disorder, or depression; only if it is without such a 'cause', is it acceptably panic disorder. These difficulties are less of a problem for ICD-9, for at least two major reasons: though this follows a similarly hierarchical scheme, it has a relatively lighter use of operational criteria, leading to distinctions that are often less narrow than DSM-III, and it allows aetiology as a basis of classification.

The present research problem is twofold: what sort of causal models should be used in guiding research thinking and in building hypotheses, and what elements actually constitute proof of causality. Though epidemiology continually debates a series of differing multi-causal models, noting that most medical explanations demand an interactive web, or network of causality, doctors are generally most comfortable with single, direct causal effects. Such a preference for direct, uni-causal thinking is not surprising, and is a legacy of the enormous triumphs of germ theory and 19th-century medicine, when the discipline started to become scientific, and reliable therapeutics became possible. The explication of uni-causality reached its fullest declaration in Koch's Postulates, adapted, with modifications, from his teacher Henle: the causative organism is always found with the disease; the organism is not found with any other disease; the organism, when isolated from other organisms that have caused disease, cultured over generations, causes the disease anew in an experimental subject; the organism is then isolated from this newly diseased subject (Koch, 1932; Susser, 1973). Though Koch, with other 19th-century clinicians, understood the relation between agent, host, and environment as a complicated set of genetic and acquired characteristics, having both distal and primary causes, medicine has remained enthralled with uni-causal, direct effects. Although these are relatively rare, they are still frequent enough to occasion great public comment. Diethylstilboesterol and vaginal adenocarcinoma is one example; the search for the 'single' AIDS virus is another. Public and media preference for such uni-causal thinking is also evident.

Such preference is not merely historically understandable, but psychologically credible. Multi-causal models produce results that are inherently harder to accept. The results of the Framingham study, where a host of different factors 'explain' only a minority of the variance of coronary disease, with many of these variables themselves probable proxies for more directly causative variables, leaves many people unsatisfied. The shift from these contingency models to log linear regression models, where individuals are assigned aggregate statistical 'risk scores', is that much more removed from daily practice, and does not provide physicians with the emotional certainty they feel about the causes of infectious disease. This same problem occurs throughout medical disciplines: categorical disease syndromes like hypertension and congestive heart failure are not very removed in clinical understanding or general treatment approaches from syndromic equivalents in psychiatry, like schizophrenia.

Psychiatry still possesses the legacy of Freud who, as a student of Brentano, and through him of other philosophers like Schopenhauer, Feuerbach, Fichte, Schelling, and Kant, held to a view of causality that was multi-dimensional and multi-causal in nature. Over time, Freudian models of the psyche changed from topographical, to structural, to metastructural, always demanding relatively sophisticated causal reasoning. However, the specificity of the underlying elements, and the actual rules of their causal connection, were not defined, making experimentation difficult. With the biological revolution in psychiatry, a positivist, linear approach has taken the place of the more dialectical ideas. Not only are simple models of causality used, but often causality is inferred from treatment effect. Given the large number of unknown intervening variables, these conclusions are unwarranted. The implication (Kendell, 1975) that such causal thinking was banished forever from medical research has proven premature, at least in the United States.

In present-day psychiatry, models of causality seem to operate around three separate schools—the biological, the psychological, and the social. Attempts to fuse them all in a single heuristic explanation, as in Engel's bio-psycho-social model, are relatively rare in clinical research. The psychosocial axes of DSM-III are infrequently considered or utilized in clinical trials, though they may sometimes have prognostic import. It is possible that some common ground exists between all three camps, with all potentially accepting some final, mechanistic 'common pathway' in the brain. However, they all disagree on how this final state is accomplished, and on what should be done when it appears.

The debate can be illustrated briefly by looking at the different theories of the aetiology of depression, where the present classificatory schemes in DSM-III and ICD-9 attempt to satisfy all camps. The biological camp argues that 'biological' treatments like ECT and antidepressants are clearly effective in dispelling the syndrome; and by equating treatment effect and aetiology, extend their ground by declaring that these aetiological elements 'must be biologic' in nature. (Freeman, 1982; Schatzberg *et al* 1982; Van Praag, 1982). The increased load of depression in first-degree relatives and families is also described as supporting such a biological view (Leckman *et al,* 1983).

Psychological theorists counter that not merely antidepressants, but cognitive therapy is a useful treatment for depression, with results that are equivalent, or even better (Rush, 1983). Behaviourists devise similar general models for the aetiology and treatment of depression (Marks, 1981). Social theorists not only point to life events as aetiological, but describe the different prevalence rates in the depressed population, as related to sex, social class and age (Brown & Harris, 1978). It is also pointed out, as in the debate on schizophrenia and the Danish adoption studies, that clustering in families does not immediately support genetic explanations for schizophrenia, since families may be viewed as transmitting the disease behaviourally rather than biologically (Lidz & Blatt, 1983; Kendler, 1983).

Each school seems to desire a certain causal congruence, a 'homogeneity', with other illnesses, as well as depression. There is a hope that the diagnostic classifications used will accurately describe unitary phenomena; each classification will be the result of a single form or nature of cause, with a homogeneous presentation and a form of therapy guided by the clear nature of the aetiology. This is an old hope, and the Kraepelinian system was based on similar beliefs (Kendell, 1975). Such reasoning resolutely denies the fact that in medical illnesses, multiple effects may stem from a single cause, or that multiple causes may together produce a single effect. Given this attempt at unitary hypothesising, we can begin to understand Virchow's sour reaction to Koch's discovery of the tubercle bacillus. Koch declared that scrofula, tuberculosis, and consumption were all caused by the same agent, but how could such an extraordinary series of differing presentations flow from the same single cause? That single causes may have multiple effects, and many causes together only a single or no effect is just the sort of consideration psychiatry must now heed.

Causal thinking is sometimes less than ideal within psychiatric epidemiology. In the otherwise excellent paper by Boyd *et al* (1984), pointing out the precariousness of exclusionary criteria in DSM-III, it is declared that for disorder A to cause another disorder B, one of two 'central principles'—a *sine qua non* to prove such causality—is that 'one would need to show that the disorders wax and wane together'. This does not necessarily follow; symptom complexes may wax and wane together, and not be causally related, or may wax and wane apart, as in syphilis or tuberculosis, yet have the same cause; the mere conjunction of two phenomena does not imply causality. Rather, medical causality is more characterized by directionality and asymmetrical time-order, than by simultaneous events. The whole stimulus response model of causality implies an antecedent cause, and some lag-time prior to effect.

The conjunction of two phenomena may appear for many reasons (Susser, 1973). It may happen fortuitously, simply as a result of chance. Phenomena may be contemporaneous by virtue of functional interdependence, where one variable cannot exist without the other; in this case, causality is not implied. Separate phenomena can be contemporaneous by virtue of a 'common complex'; many variables in epidemiology occur without either being necessary to one another or inter-dependent, e.g. high pollution levels are often found in combination with crowding and poor housing. Finally, two phenomena may be contemporaneous and 'wax and wane' together because they are both effects of a common cause, e.g. in Graves' disease, the course of thyrotoxicosis does not follow the course, with or without treatment, of the concomitant ophthalmoplegia; by Boyd *et al*'s definition, these two entities would be considered separate diseases.

Although aetiology is the desired underpinning of most medical classification systems, the present lack of clear causal models for just about any diagnosis means that psychiatry must be nosologically cautious. It must consider causality both from a multi-causal angle as well as from that of multiple, multi-levelled interactive systems. The complexity of approach this demands should, however, not cause psychiatry to give up hypothesis testing—a process deliberately eschewed by DSM-III, and not particularly well engendered by ICD-9. But when thinking in causal terms, it should be useful to look at various modes and models of causality.

The matter of what constitutes proof of causality, and what causal models to use was dealt with by Yerushalmy & Palmer in the 1950s and has been considerably refined since then (Yerushalmy & Palmer, 1959; Hill, 1965; Feinstein, 1979; Walker & Holford, 1978). Research workers should always consider whether variables are potentially necessary, sufficient, or neither. Even in linear models of single independent and dependent variables, there are four conditions where independent variable X may cause dependent variable Y: (1) X is necessary and sufficient to cause Y; (2) X is necessary but not sufficient to cause Y; (3) X is not necessary but sufficient to cause Y; (4) X is neither necessary nor sufficient to cause Y. Considering also (as is often the case in the natural sciences) that a particular cause may give rise to more than one effect, a fifth category may be added, where X may cause Y1, Y2, Y3, to Yn.

Given multiplicity of causes and effects, several relationships are possible between two variables, and far more relationships are possible between three variables. Taking the simplifying assumptions of neutrality of time order and uni-directionality of cause and effect, systems of variables can be ordered in an extraordinarily large number of ways. The number of possible causal chains, even in the simplifying linear case, is the number of variables factorial (ten variables can be ordered 10!, or 3,628,800 ways). There are yet further considerations for the causes and effects studied: (1) Causative variables may be antecedent to the cause and effect being looked at. (2) Other variables may intervene between the cause and the effect. (3) Different variables may moderate between cause and effect, with widely varying results; reversing the trends of causative variables, or synergistically increasing them, even suppressing them. (4) Variables may act as components of other causal variables. (5) Single variables may be the cause of multiple effects, whose sequential order of appearance falsely calls forth the researcher to see the connection between these effects as itself causal.

There is a marked complexity of the chain of causality for most medical phenomena, which is really enormous in the psychiatric context, where the chains of causality are long, inflected by a series of major causal classes (social, genetic, biological, intra-psychic, etc.), and in all probability, highly interactive. One way to begin to conceptualise causality for such phenomena is to consider the system devised by Rothman (1974; 1978).

Rothman posits the need for both sufficient and necessary causes, but not in the way that is commonly considered. There is a linguistic difficulty in defining 'cause'; one seemingly tautological definition is to say it is an act or natural state which allows or initiates, alone or in conjunction with other causes, an effect. However, a cause may itself consist of a constellation of components, which linguistically are also referred to normally as causes. The question is how to define when a cause is necessary or sufficient.

A 'sufficient' cause is defined as a constellation of components which will inevitably produce the expected effect and a series of sufficient causes, potentially reaching infinity, may in fact provoke disease. If there is a component cause which is a member of every sufficient cause, that component is a necessary cause. Some necessary causes in medicine are tautological—an appendix is needed if one is to have appendicitis—but other necessary causes are not tautological: cholera cannot occur without the cholera vibrio. Medicine is often at its most effective, when it can identify and treat such necessary causes, while prevention is probably most effective when it is aimed at necessary causes. Yet if a cause is a component of a large number of sufficient causes, its prevention may still be exceedingly effective.

From this model of a multiplicity of sufficient causes, an understanding of independence, antagonism, and synergy of causes is possible. If a component cause is found to act through one, and one sufficient cause only, its effects will probably be independent of other effects: synergy and antagonism will not apply. However, if two components of the same sufficient cause occur simultaneously, this may well lead to synergistic effects. Similarly, an agent which dissipates or negatively affects components of a sufficient cause may be said to act antagonistically.

Given that no clear causal variables are available in psychiatry, with the possible exception of organic syndromes, causality must be assessed carefully. Causal variables nest within and among other causal variables; given the variability of human behaviour, the network to study is indeed huge. Given this wide field, classificatory goals should be tempered by caution.

Despite their present usefulness, their clear advantages over previous classificatory schemes, and their built-in mechanisms for revision, both DSM-III and ICD-9 attempt to fill a very tall order. Relying on the specification of clinical phenomena alone, both classifications imply that such clinical phenomena will somehow be useful for the varied purposes to which psychiatric nosologies are put. Historically, there are at least three major uses of psychiatric nosologies: to define causality; to predict prognosis, with or without treatment; and to describe public health needs and the impact of services. Classifications which would be homogeneous for the purposes of aetiology, prognosis, treatment, and public health services (the latter involving the social cost of mental illness) are as yet unachievable.

Since the development of the Research Diagnostic Criteria, psychiatric nosology has progressively moved toward prognosis as the major classifying variate (Goodwin & Guze, 1984). Without stratification along prognostically homogeneous groups, clinical research, especially clinical trials, are inevitably biased (Feinstein, 1972a). Aetiology, however, is a different matter: even assuming uni-causal models, which psychiatric research almost never can, causes have very different effects in different individuals; the behavioural phenomena that result need not look the same in everyone, and almost surely will not. Similarly, public health needs vary markedly with social, political, and economic factors. What is 'disabling' in one population, may be a minor irritation in another. Essen-Moller (1971, 1973) created typologies which, however idiosyncratic, demanded separate classifications for symptomatology and aetiology, yet wholly separate classifications schemes may not be the answer.

Prognosis and prognostic stratification should remain the major goal of diagnostic classification, because it is necessary for both clinical practice and clinical research (Kendell, 1975). However, supplemental taxonomies are also needed. If these are developed for research on aetiology and public health needs, such difficulties may be obviated. The research goal should be to stratify patient populations into homogeneous groups (Feinstein, 1972b); a prognostically homogeneous sample can be split and used to compare the results of therapeutic manoeuvres. A population group that has experienced one or more of an identified putative cause can be followed over time, to note possible effects. With sub-typing of psychiatric populations along prognostic, aetiological, and public health lines, the results of psychiatric research should ultimately become clearer.

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Matthew J. Edlund, MD, MOH, *Assistant Professor, Department of Psychiatry, University of Texas, Houston, Texas 77225, USA.*

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Brief Reports

Clovoxamine and Doxepin in Major Depressive Disorder: A Double-Blind Controlled Trial

Clovoxamine, an inhibitor of neuronal uptake of both serotin and noradrenaline, was compared with doxepin in depressed patients over four weeks. Antidepressant efficacy was comparable for both drugs, but clovoxamine might have a special degree of efficacy for patients with more severe depressive illnesses.

This paper reports a multi-centre double-blind controlled study of clovoxamine versus doxepin in depressed patients. Clovoxamine fumarate is a compound in the series of 2-aminoethyl oximethers of aralkylketones; in animal pharmacological studies, it was found to inhibit neuronal re-uptake of both serotonin and noradrenaline, *in vitro* and *in vivo,* while having slight effects in blocking dopamine uptake (Classen *et al*, 1978; Richelson & Pfenning, 1984). Chronic administration results in a down-regulation of the beta adrenergic system (Bradford *et al*, 1985) but the drug has virtually no anticholinergic sedative, antihistaminic, or amphetamine-like stimulating effects, and causes no inhibition of monoamine oxidase (Richelson & Nelson, 1984).

Tolerance studies in healthy volunteers confirmed the absence of anticholinergic effects and established its non-cardiotoxic profile (Robinson & Doogan, 1982). Open clinical studies in depressed patients indicated a clear anti-depressant action of clovoxamine (Wright *et al*, 1981; Freeman *et al*, 1982; Calanca *et al*, 1983). Subsequently, double-blind studies with several tricyclic anti-depressants showed that clovoxamine did not show unexpected or potentially dangerous reactions; unwanted signs and symptoms were usually mild. In these controlled studies, there were no significant differences between the groups for incidence of unwanted effects, except in one comparison with amitryptiline, where anticholinergic effects were fewer on clovoxamine (Gelenberg *et al*, 1985). Clovoxamine showed significantly more relief of anxiety as a component of depression than did placebo, while no unexpected or clinically significant laboratory changes were observed. This present study was designed to compare the relative efficacy, safety, and tolerance of clovoxamine and doxepin.

Method

Subjects

The study was conducted at two hospitals. Patients included had presented with an established diagnosis of major primary depression (unipolar or bipolar). The age-range was 18 to 70 years. Subjects had to have a persistent alteration of mood which exceeded customary sadness, could not be raised by social contact, and was not attributable to any life event; they were further selected for possible entry on the basis of meeting four of the diagnostic criteria of Feighner *et al.* All patients had to score at least 15 points on the first 17 items of the Hamilton Rating Scale for Depression (HAMD). The following were excluded from entry into the study: pregnant women or females of childbearing potential who were not taking adequate contraceptive measures; patients with other psychiatric illness or any significant organic disease; those with drug addiction (including alcohol); patients with an initial depression lasting less than two weeks; those with glaucoma or urinary retention; and out-patients who were regarded as dangerous to themselves or others.

Patients receiving the following compounds or therapy were not admitted to the study: electroconvulsive treatment (ECT) within the past four weeks; lithium within the past four weeks; MAO-inhibitors within the past two weeks; other anti-depressants within the past week; and any short- or long-term medication which could not be discontinued and/or might interact with the study drug.

Before study treatment, there was a drug-free wash-out period of one day to four weeks; the duration of this period depended on the type of medication that had previously been given for the current episode: i.e. MAOI—two weeks, lithium—four weeks, ECT—four weeks, other anti-depressants—one week. If no antidepressant medication had been administered, patients could enter the study after the baseline evaluations were completed and laboratory results were known. During the wash-out period or in the treatment administration weeks, no other medication was to be given, with a few exceptions. The dosage strength of clovoxamine was 50 mg, while doxepin was supplied in capsules containing 25 mg.

The study drug was to be administered in three divided doses per day,, at breakfast, lunch, and at night. The recommended daily dosage was 3–6 capsules per day (equivalent to 150–300 mg clovoxamine or 75–100 mg doxepin). The maximum permitted dosage was eight capsules per day. On day 1, a starting dose was given of one capsule, three times daily. From day 2 to 28, the dosage could be adjusted according to the patient's clinical response. After 28 days, medication was tapered off over three days, unless the patient was allocated to the long-term treatment extension. The study was carried out primarily on an out-patient basis, although a period of admission did not exclude any patient.

The study medication could be interrupted or terminated at the patient's request, or if the investigator considered it necessary, before conclusion of the four-week study programme.

During the wash-out period (i.e. week 0) and the four drug administration weeks, only the following concurrent drugs were allowed: benzodiazepines, antibiotics, non-narcotics, analgesics, antacids, and aperients.

Assessments

The HAMD, 17-item version, and Clinical Global Impression Scale (CGI) were used as the primary efficacy scales. Daily dosage, vital signs data, and concurrent medication were recorded throughout the study. Laboratory data were obtained during the wash-out period and at weeks 2 and 4. ECGs were done before and after the treatment period.

Statistical methods

The following methods were employed: (a) two-sample Wilcoxon test with adjustment for ties for between group comparisons of quantative and ordinal variables; (b) chi-square test for all qualitative variables and for ordinal variables in 2 x 2 contingency tables; (c) Fisher's exact test employed for 2 x 2 tables with small expected cell frequencies; (d) the sign test, signed-rank test, M-trend test for general and monotone changes over time within groups for vital signs and laboratory test results. Only two-sided tests were used in this analysis. All P-values were reviewed, and only those related to findings of clinical importance (whether significant or not) selected for comment.

Results

Thirty-four patients received the study drugs—17 in the clovoxamine and 17 in the doxepin group. There were 26 females and eight males, evenly distributed between the two treatment groups. Their ages ranged from 20 to 67 years; the mean age was 45 years for the clovoxamine group, and 48 for the doxepin group. All patients had an established diagnosis of primary depression. In the clovoxamine group, there were 14 unipolar endogenous and three non-endogenous depressed patients, while in the doxepin group there were 13 unipolar endogenous and four non-endogenous depressed patients. Demographic data for the two groups were comparable. The mean length of the current depressive episode was 6.6 months in the clovoxamine and 4.8 months in the doxepin group. Study medication had to be terminated before 28 days of drug administration in five clovoxamine patients (all for intolerance) and in one doxepin patient, because of insufficient therapeutic effect. There appeared to be good compliance with study drug intake, as checked by tablet counts. No statistically significant differences in intake of concurrent medication were found between the two groups; drugs prescribed for headache and constipation increased in both groups towards the end of treatment period. The pre-treatment comparability on the total HAMD score was good (P-value 0.72).

The Hamilton Rating Scale for Depression

Patients in both groups showed a good response to treatment, as measured by HAMD. The clovoxamine group improved by 48%, the doxepin group by 52%; there was no statistically significant difference between the two groups at any time with respect to these scores. However, a statistically significant difference between the groups was found for factor 1 (anxiety/somatisation) at week 1, in which doxepin was superior to clovoxamine ($P=0.021$). Also, for the somatic symptom item (gastro-intestinal), there appears to be a trend throughout the study period in favour of doxepin.

Clinical Global Impression Scale

Prior to treatment, the severity scores of the two groups of patients who entered the study were comparable, and there were no marked differences between the groups at any time. However, when the two groups of patients who qualified for the end-point analyses were considered, a significant difference is found (P-value 0.027), i.e. the clovoxamine treated group was more depressed at the start of the study period than the doxepin group. At the end of treatment, there was no difference between the groups: in the clovoxamine group, mean severity over the treatment period fell from 5.2 to 3, while the comparable figures for the doxepin group were 4.3 and 2.8.

The final rate of responders, defined as the proportion of patients who were (very) much improved according to the investigators' global impression was 73% for the clovoxamine group versus 88% for the doxepin group. However, there was a sizeable difference between the groups for the patients' own evaluation of change: 97% of patients in the doxepin group regarded themselves as (very) much improved, against 50% of the clovoxamine-treated patients.

Heart rates

No statistical difference was seen between the treatment groups at any time-point, though the clovoxamine group showed a mean increase in heart rate of four beats per minute, over the study period.

Blood pressure

This was only measured in a sitting position. There was a significant trend of a decrease in systolic blood pressure in the doxepin group ($P=0.0143$). No statistically significant difference between the two groups was found.

Electrocardiograms

In both groups, normal pre-treatment ECGs remained normal at week 4.

Body weight

The clovoxamine group showed a mean weight gain of 2.4 kg over the four-week treatment period, against 1.2 kg increased for the doxepin group. This difference failed to reach statistical significance. None of the observed variations in grouped laboratory results appears to be of clinical relevance; any changes were within the normal ranges.

Treatment-emergent signs and symptoms

Treatment-emergent signs and symptoms (TESS) are those complaints present at pre-treatment but worsening during the study medication period, or complaints appearing during that period. In the clovoxamine group, all 17 patients showed TESS, whereas in the doxepin group, the incidence rate was 14 out of 17 patients (Table). The incidence rate of most TESS was equally divided over both treatment groups, but the rate of headache was higher in the clovoxamine group. There was a slightly higher rate of anticholinergic symptoms in the clovoxamine group, where unwanted effects led to the discontinuation of treatment in five patients: one of these developed multiple ventricular ectopics, particularly on standing, during the two days she received the drug. Another of these patients suffered from severe vomiting and reported fainting during the first treatment week; in both cases, the complaints disappeared soon after medication was stopped. One patient on doxepin dropped out because of lack of efficacy, and was also suffering from severe dry mouth.

TABLE
Treatment-emergent signs and symptoms reported by at least 10% of patients

Score Category	*Number of patients with complaint*	
	Clovoxamine group	*Doxepin group*
Headache	9	3
Somnolence	11	9
Dizziness	7	7
Constipation	7	6
Dry mouth	7	5
Nausea	6	4
Tremor	6	5
Sweating	6	3
Accommodation abnormal	5	4
Paresthesia	3	2
Pain (site)	1	3
Urinary retention	1	3
Vomiting	3	1

Discussion

The design was sufficient to evaluate the main objectives of this study, which were to compare the antidepressant effect of clovoxamine and doxepin, and to evaluate the side-effect profiles of the two drugs. The efficacy results from the HAMD and CGI rating scales suggest that both study drugs have an antidepressant effect. Considering the end-point results, the clovoxamine group showed a 48% improvement in HAMD scores, whereas this was 52% in the doxepin group. The investigators scored 73% improvement for the clovoxamine patients and 88% for the doxepin group, while the patients scored 50% versus 94%. An explanation for this discrepancy may be derived from the CGI end-point severity analysis. Here, the clovoxamine group had a significantly higher entry score, which means that the clovoxamine group was more severely depressed at pre-treatment. Three out of the four subjects with psychotic depressive symptoms who were treated with clovoxamine improved significantly on that drug alone. No clinically relevant changes were seen in the safety parameters.

It was concluded that whilst clovoxamine is an effective anti-depressant, with a degree of efficacy comparable to that of the established tricyclic compounds, it has no overall advantages when compared with doxepin. However, it might have a special degree of efficacy in patients with more severe depressive illnesses; this question remains to be investigated further.

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G. J. Lodge, MB, MRCPsych, *Consultant Psychiatrist, Roundway Hospital, Devizes, Wilts. SN10 5DS.*

*Hugh L. Freeman, MA, MSc, BM, FRCPsych, *Consultant Psychiatrist, Hope Hospital, Salford, M6 8HD.*

*Correspondence

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Prolactin Response Induced by ECT and TRH

The prolactin response after ECT in ten female melancholic patients correlated significantly to their prolactin response to i.v. TRH. These findings may suggest an underlying common mechanism between TRH and ECT regarding their PRL releasing properties.

Increase in serum prolactin (PRL) represents one of the most consistent findings of the immediate effect of electroconvulsive therapy (ECT), and this response has been associated with the seizure and the location of the electrodes rather than with non-specific phenomena, such as stress and/or anaesthesia (Ohman *et al*, 1976; Whalley *et al*, 1982; Swartz & Abrams, 1984; Papakostas *et al*, 1984). Thus, the study of PRL secretion as a biochemical marker of the seizure, which is postulated to be crucial to the therapeutic outcome (Kendell, 1981), can be considered a useful tool in exploring underlying ECT mechanisms.

Comparison of the pattern of the ECT-induced PRL secretion to that induced by other PRL-secretagogue stimuli, when they are applied to the same population, can add some relevant information. This approach has been adopted by Arato & Bagdy (1982), who compared the pattern of the ECT-induced PRL response to that induced by haloperidol; in this study, we compared this pattern to that induced by the thyrotropin-releasing hormone (TRH).

Method

Ten female patients referred for ECT and meeting DSM-III criteria (APA, 1980) for major depressive disorder, melancholia-type, were studied. They were diagnosed independently by two psychiatrists (YGP, GNP) on the basis of standard clinical interviews and patients' records. The age range was 40–69 years. Patients were free of psychotropic or any other drugs known to affect PRL secretion, for at least one week before ECT administration, with the exception of low doses of benzodiazepines (flunitrazepam) given at bed-time. The TRH test was performed at 0900 hr after an overnight fast, with the subject recumbent while blood was taken through an indwelling needle, immediately before and 20, 40 and 60 min after the injection of TRH (0.4 mg intravenously as a bolus). During the first bilateral ECT session, which took place two days later at 0900 hr, blood samples were drawn immediately before the electrical stimulus was delivered, and 5 and 15 min after the induction of a seizure monitored by the 'cuff method' (Fink & Johnson, 1982). The optimal time for observing maximum serum PRL changes is 15 minutes post-ECT (Swartz & Abrams, 1984) and the period between 15 and 30 min after intravenous TRH administration (Jackson, 1982). The standard anaesthesia procedures, the characteristics of the electrical stimulus, and the assessment of PRL are described elsewhere (Papakostas *et al*, 1984).

Results

The peak PRL responses occurred at 5′ (five patients), or 15′ (five patients) after ECT, and at 20′ (nine patients) or 40′ (one patient) after TRH. A significant positive correlation ($r=0.79$, $P<0.01$) between the ECT- and the TRH-induced Δmax PRL response was found (Δmax PRL:peak minus baseline value).

This correlation becomes even stronger by calculating the mean PRL increase at 5 mins and 15 mins post-ECT, and 20 mins and 40 mins post-TRH over the baseline ($r=0.82$ $P<0.01$, see Figure).

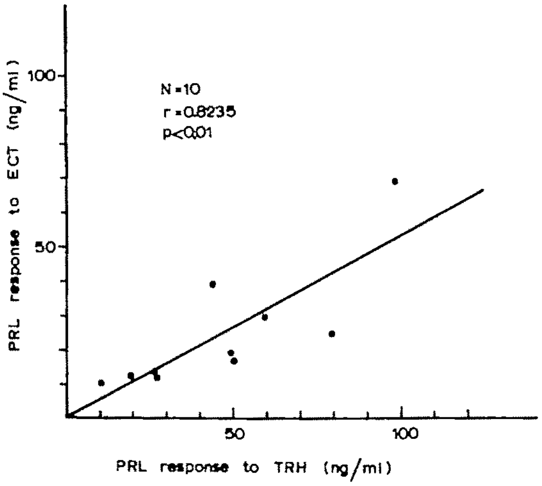

Fig. 1 Prolactin (PRL) response to electroconvulsive therapy (ECT) and thyrotropin-releasing hormone (TRH)

Discussion

The pattern of haloperidol-induced PRL increase is different from that induced by ECT (Arato & Bagdy, 1982), or TRH (Hays & Rubin, 1981), research findings suggesting that different mechanisms are underlying these responses. In this study, the PRL responses after ECT correlated significantly to those produced by TRH, the findings indicating a functional similarity between the two stimuli concerning their PRL-releasing properties, and possibly a final common mechanism accounting for these responses. However, the exact mechanisms mediating these responses are unknown. Intravenous TRH is thought to cause PRL secretion through direct stimulation of the lactotropes (Jackson, 1982). Although there are no comparative studies, previous reports indicate a faster PRL peak after ECT than after TRH administration (Swartz & Abrams, 1984; Jackson, 1984), which may suggest that some intermediate processes delay the final PRL-releasing effect of TRH. Release of TRH during ECT might be one explanation accounting for the PRL secretion, but Whalley *et al* (1982) were unable to detect any TRH changes during ECT. The notion of the TRH involvement is also not supported by the established absence of a concomitant TSH secretion during ECT (Thorell & Adielson, 1973; Whalley *et al*, 1982), as would be expected if such a mechanism were present. However, a dissociation between TSH and PRL, as it occurs with ECT, does not exclude TRH involvement, since such a dissociation can occur under certain circumstances (Winokur *et al*, 1984). According to these authors, repeated TRH administration resulted in a diminished TSH, but not PRL response. Thus, more specific measures of neurotransmitter function may be helpful in exploring the nature of the positive correlation between ECT and TRH-induced PRL secretion, which was found in this study.

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Yiannis Papakostas, MD, *Senior Lecturer in Psychiatry*

Manolis Markianos, PhD

George Papadimitriou, MD, *Lecturer in Psychiatry*

*Costas Stefanis, MD, *Professor and Chairman, Athens University Medical School, Department of Psychiatry, Eginition Hospital, 74 Vas. Sophias Ave., Athens, Greece.*

*Correspondence

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Comparison of the Prophylactic Action of Flupenthixol with Placebo in Lithium Treated Manic-Depressive Patients

A double-blind cross-over trial of depot flupenthixol in recurrent manic depressive psychosis was carried out. All patients continued on lithium. Eleven patients completed the two-year trial. Flupenthixol appeared to have no prophylactic effect.

Flupenthixol, a potent neuroleptic drug, is widely used in the treatment of schizophrenia. In the late 1960s, Sonne (1966) and Reiter (1969) reported that it relieves moderate symptoms of acute depression. In an open trial, Ahlfors *et al* (1981) compared the prophylactic effect of flupenthixol against lithium in manic-depressive patients. Flupenthixol appeared to have no prophylactic effect against recurrent depression, but was associated with significant falls in the frequency and duration of manic episodes. Naylor & Scott (1980) described five recurrent bipolar manic-depressive patients in whom depot injections of fluphenazine or flupenthixol appeared to be useful in preventing relapse.

Most manic-depressive patients benefit from prophylactic lithium, but despite this therapy, a significant number continue to suffer frequent recurrences of affective illness. This group present major problems in management, and often suffer considerable social handicap. Except perhaps for carbamazepine, there is no drug other than lithium of proven prophylactic use in bipolar manic-depressive illness, so that clinicians frequently resort to depot preparations of major tranquillisers. The present study was designed to investigate the prophylactic effect of flupenthixol in patients who continued to relapse, despite prophylactic lithium.

Method

Patients: All patients considered for inclusion had bipolar manic-depressive illnesses; all but two had more than one hospital admission in the preceding two years, and all had displayed typical depressive and manic or mixed symptomatology. They all had been receiving lithium regularly for at least two years prior to the trial and had suffered frequent relapses of affective illness whilst on this. Three patients were on treatment with thyroxin, and one was a diabetic receiving chlorpropamide.

Trial design: No restriction was placed on other prescribed medication. Lithium dosage was adjusted to keep the plasma level within the therapeutic range (0.6 to 1.2 mmol/litre). Patients were randomly allocated to treatment with 20 mg flupenthixol injections (nine patients) or placebo injections (six patients). Injections were administered by four-weekly intervals for one year, at the end of which the subjects were switched to the alternative preparation. The trial was double-blind and in order to avoid extrapyramidal side-effects revealing the nature of the medication, all patients received benzhexol throughout.

At four-weekly intervals, the patient's affective state was assessed on a simple four-point rating scale (Coppen *et al*, 1976) and serum lithium levels were estimated. The patient's weight, side-effects, dates of inpatient admissions, duration of affective disturbances without admission, and other psychotropic medication were also recorded. The trial continued even if a patient was admitted to inpatient care. From the data on the clinical ratings throughout the trial, the Affective Morbidity Index was calculated (Coppen *et al*, 1976). Case notes of each patient were examined for details of the previous psychiatric history.

Results

Fifteen patients were initially included—four males and 11 females; four patients (three males and one female) failed to complete the trial and all of these dropped out within the first three months (two were receiving placebo, two flupenthixol). Ten females and one male completed the trial. The mean age of the patients at the beginning of the trial was 49.3 (range 27 to 62) years.

The number of days the patient spent as an inpatient during both the placebo and active treatment periods and in the two years prior to the trial were calculated (Table). The total number of days spent in hospital during the trial in either active or placebo periods was less than (approximately half) the average number of days spent in the two years prior to the trial, but there was no difference in hospital days between the active and placebo periods. It was impossible to quantify accurately other psychotropic medication given during the trial; which consisted of benzodiazepine night sedation, a variety of antidepressant drugs and, rarely, phenothiazines; however, there was no evidence that the nature or amount of such medication given differed between the placebo and active phases.

The Wilcoxon Test was used to compare the Affective Morbidity Index in placebo and active periods. Patients were significantly better ($P<0.05$) during the placebo-treated period than during the flupenthixol-treated period.

The clinical ratings of mania during the placebo and active periods and the similar ratings of depression were separately computed and compared: six out of eight patients had lower (less severe) depressive ratings during the placebo period than during the flupenthixol period, but no statistically significant differences between the two treatment periods emerged. There was no suggestion that flupenthixol had any differential effect in the prophylaxis of either mania or of depression. The mean plasma lithium concentration during the placebo period was 0.85±0.10 mmol/litre, during the active period was 0.83±0.11 mmol/litre, and during the two years before the trial was 0.80±0.08 mmol/litre. These levels were not significantly different.

TABLE

Number of days the patient spent in hospital during the placebo and active treatment periods and in the two years prior to the trial

	Placebo year	*Active drug year*	*Mean for 2 years before trial*
1 (P,A)	125	0	142
2 (A,P)	0	0	0
3 (A,P)	0	0	137
4 (P,A)	0	0	0
5 (P,A)	0	0	54
6 (A,P)	0	0	123
7 (P,A)	0	0	74
8 (P,A)	0	0	30
9 (A,P)	45	255	59
10 (A,P)	291	257	273
11 (A,P)	0	0	83

(A,P) = Active treatment followed by placebo.
(P,A) = Placebo followed by active treatment.

Discussion

Negative trials need to be interpreted with caution, since they may simply have failed to show a real difference. However, the present study suggests that patients were worse on flupenthixol than on placebo. This difference may have been spurious or may be a reflection of side-effects of flupenthixol—perhaps extrapyramidal side-effects were important, despite treatment with benzhexol. It is unlikely that flupenthixol caused depression, since it is reported to have an antidepressant effect in acute depression. The most notable finding was how much better the patients were during the trial period than during the preceding two years, and this improvement is difficult to explain. There was no evidence that the lithium levels were better controlled during the trial, and they did not differ significantly between the trial and pre-trial periods; Coppen *et al* (1984) have shown that reducing lithium levels may in fact improve prophylaxis. There was probably more medical attention during the trial, and attendance for a monthly injection may have had a powerful placebo effect.

This study thus provided no evidence that depot injections of flupenthixol are of therapeutic value in manic-depressive patients who relapse frequently despite lithium therapy.

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J. Esparon, MB, ChB, *Registrar, Murray Royal Hospital, Perth.*

J. Kolloori, MB, ChB, *Registrar, Royal Dundee Liff Hospital.*

*G. J. Naylor, MD, BSc, FRCPsych, *Reader in Psychiatry, Royal Dundee Liff Hospital, Dundee DD2 5IF.*

A. M. McHarg, MB, ChB, MRCPsych, *Consultant Psychiatrist, Royal Dundee Liff Hospital.*

A. H. W. Smith, MB, ChB, MRCPsych, *Consultant Psychiatrist, Royal Dundee Liff Hospital.*

S. E. Hopwood, MB, ChB, MRCPsych, *Senior Registrar, Royal Dundee Liff Hospital.*

*Correspondence

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A Case of Parietal Lobe Atrophy

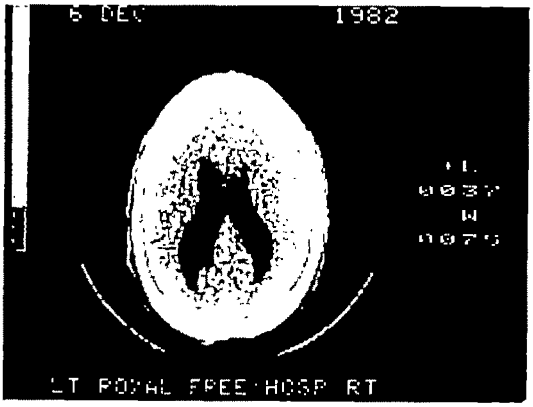
Bilateral parietal lobe atrophy was revealed by CT scan in a 48 year-old man, with a history of learning difficulties since childhood, encopretic up to the age of eight, and left-handedness. Nevertheless, he earned his living as a skilled potter, though unable to cope with the administration of the business.

The inferior parietal cortex of the human brain is concerned with the integration of information both within and between different sensory modalities (Luria, 1973). Lesions of this area may produce a wide variety of subtle defects of function including dysgraphia and dyslexia, dyscalculia, dysphasia, constructional apraxia, right-left disorientation, and finger and visual agnosias (Lishman, 1978; Benton, 1961).

Case History

A 48 year-old male presented complaining of difficulty in reading and inability to do even simple arithmetic; these problems had been apparent since childhood. There was no family history of learning difficulties, both parents and the patient's three siblings having followed professional careers. There was no history of birth trauma, convulsions, serious illness, or head injury, but the patient was encopretic until the age of eight. He was considered to be educationally subnormal, though his parents found this a difficult label to accept, and moved him around several different schools; the effect of this disruption was to deny the patient any remedial teaching until his early teens, when he underwent some basic literacy and numeracy tuition. He became interested in pottery, becoming sufficiently skilled in the craft to earn his living from it throughout his adult life; the business had been administered by his mother, now in her mid-seventies. The presentation in middle age with difficulties that had dogged him since childhood was undoubtedly manifested by his anxieties over his inability to administer his business, should his mother die to fall ill.

General and neurological examination revealed no abnormality; there was no obvious asymmetry of the face or bodily configuration. He was found to be left-handed, though all other family members are right-handed. IQ scores on the Wechsler Adult Intelligence Scale were 89 (verbal and 72 (performance): arithmetic skills were limited to addition and subtraction of single figures while reading and spelling were at the six-year level of attainment, and featured reversal of letter order. Right-left disorientation was present, and finger agnosia was equivocal on Kinsbourne & Warrington's 'In Between Test' (1962). There was impairment of appreciation of spatial relationships and temporal sequencing. Short-term auditory and visual memory impairment were present, but overt constructional apraxia, dysphasia, and dysgraphia were not present, and eye-hand co-ordination was good. He was observed at work, and was seen to have good manual dexterity and to be a skilled potter. The results were thought to be suggestive of bilateral parietal lobe dysfunction. A CT scan revealed a bilateral enlargement of the posterior part of the lateral ventricles and associated parietal atrophy. (See Fig. 1, which is a photo of the CT scan).



CT scan showing bilateral parietal atrophy.

Comment

Bilateral parietal lobe atrophy giving rise to such cognitive deficits has been found only extremely rarely. Critchley (1953), in a review of 46 cases of the Gerstmann syndrome, cites only one instance of parietal atrophy, also bilateral; out of the three-quarters of the cases where pathology was unilateral, neoplasm was responsible in the majority, whilst vascular lesions were the most common bilateral cause. In this case, the long history of cognitive deficit, along with childhood encopresis and the absence of any neoplasia, point towards this atrophy being present from early childhood or even being congenital. The absence of any family history of left-handedness is suggestive of this being a case of 'pathological' left-handedness (Gerron, 1980). Despite performing badly on several tests of body image, this patient is a skilled craftsman, which underlines the difficulty in predicting occupational performance by psychometric testing.

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*Paul Dedman, MB, BCh. MRCPsych, *Registrar*

Sharon Numa, BA, MSc, *Clinical Psychologist, Department of Psychological Medicine, The Royal Free Hospital, Pond Street, London NW3 2QG*

*Correspondence

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Unpredictability as a Correlate of Expressed Emotion in the Relatives of Schizophrenics

Family environment has an important effect on the prognosis of psychotic patients who are discharged from hospital to live at home (Brown *et al,* 1962; Brown *et al,* 1972). The Expressed Emotion (EE) rating technique is a reliable method of measuring certain emotional aspects of the family atmosphere (Vaughn & Leff, 1976*a*). Using this measure it is possible to predict which patients are liable to relapse if they return to the home from which they were admitted to hospital. If relatives are highly critical or too emotionally involved, the patient has a much greater chance of relapsing within nine months of discharge (Vaughn & Leff, 1976*b*), particularly if relative and patient spend a high proportion of their day in face-to-face contact or the patient fails to take medication regularly.

Relatives of psychiatric patients are usually more distressed by secondary deficits than by the active symptoms which follow from episodes of acute illness (Creer & Wing, 1975). Typically, it is daily irritations arising from domestic issues and failures in role performance, such as self-neglect, lack of motivation and social withdrawal, which cause conflict. Relatives' responses to these problems will therefore determine the usual quality of the home environment. Vaughn & Leff (1984) have noted a consistent relationship between relatives' responses to such problems and their EE profiles. Warm, non-critical (low-EE) relatives tend to be more tolerant, and cope by minimising the importance of the deviant behaviour while giving clear guidelines for what is acceptable. Highly critical or over-involved (high-EE) relatives often respond intolerantly, focusing attention on problems and joining battle with the patient in an effort to eliminate problems entirely. They also see problems as a reflection of long-standing defects in the patient's personality, whereas low-EE relatives view problems as isolated instances, or attribute their occurrence to the patient's illness, thus avoiding blaming the patient directly.

Earlier studies have suggested that pattern of communication within the families of people suffering from schizophrenia are likely to be confusing (Singer & Wynne, 1966; Hirsch & Leff, 1971) or even contradictory (Bateson *et al,* 1956). It is not clear how the EE measure relates to actual communication patterns in the home, since it is based on interviews with the relative alone; nor is it clear why the emotional attitude of a relative, expressed during an interview, is related to the subsequent relapse of the patient (Kuipers, 1979). Nevertheless, relatives' attitudes do appear to be causally related to relapse, and not merely correlated with fluctuations in the patients' level of disturbance (Leff *et al,* 1982). Moreover, there is now evidence that EE ratings do reflect aspects of the family's habitual style of interaction (Miklowitz *et al,* 1984).

No previous study has considered the mechanism by which the behaviour of relatives precipitates relapse. However, studies of cognitive deficits associated with schizophrenia have suggested that a highly stimulating environment may provoke clinical deterioration, because of the patient's limited capacity for information processing and response selection: redundant or distracting information which would be filtered out by normal subjects is given equal attention by subjects suffering from schizophrenia (Hemsley & Zawada, 1976). Such cognitive deficits could account directly for some of the positive symptoms of schizophrenia (Frith, 1979); while negative symptoms, such as slowness and withdrawal, could represent an attempt to reduce stimulation and thus avoid more disturbing positive symptoms (Hemsley, 1977). In a cognitively simple environment, where information overload is kept to a minimum, processing can be conducted at a level of efficiency similar to that of non-psychotic people (Meiselman, 1973).

The main causal hypothesis suggested by this line of reasoning is that high-EE relatives may provide a cognitively more complex home environment, by responding to difficult behaviour in ways which make it harder for psychotic patients to identify or respond to the significant parts of their communications. If relatives give ambiguous or unpredictable information about their own feelings and the kind of behaviour they expect from the patient, this may account for the higher rate of relapse among patients in high-EE homes.

We conceptualised unpredictably in two ways—firstly as an interaction effect, and secondly as an aspect of the relative's behaviour alone. This allowed us to formulate two specific hypotheses:

1. High-EE relatives may be less likely to agree with the patient about the occurrence of problems, or about their own coping behaviour, than low-EE relatives. Because the relative and patient appraise each other's behaviour differently, the relative's behaviour appears less predictable to the patient.
2. High-EE relatives may be more likely to vary their responses to problems, so that the patient can never predict the relative's behaviour with confidence.

Method

Subjects

Interviews were carried out with 28 patients with a hospital diagnosis of schizophrenia, who lived permanently with a relative or close friend.

Half of the sample were recovering from a recent acute episode of schizophrenia during which they had first-rank symptoms and were admitted to a psychiatric hospital. These 14 were interviewed before discharge, when they were well enough to complete the interview.

The other 14 patients were long-stay day patients who had attended hospital daily for over one year. They were experiencing psychotic symptoms at the time of the study.

Each subject identified a key relative or close friend with whom they usually lived and who had assumed the main responsibility for their daily support and management.

Procedure

A questionnaire was developed to assess the frequency of ten problems in daily living, and to investigate how relatives coped with these problems. Only negative symptoms of schizophrenia, such as disruption in daily routines and social withdrawal, were assessed. The questionnaire was administered to each patient individually. The patient was asked whether a particular problem had occurred within the last three months and how the key relative usually dealt with it. An equivalent questionnaire was also given to each relative.

Three common coping responses were listed for each of the ten problems, reflecting either *(a)* a warm and adaptive response, *(b)* a critical response, or *(c)* an over-involved style of coping. A fourth style *(d)*, labelled "variable", was scored when respondents reported that a relative used any of the three preceding styles, either in combination or as alternatives. A fifth category *(e)* was used when a problem evoked no response, or was carefully ignored by relatives ("passive" response).

Five filler items were included in the questionnaire to ensure that respondents were not answering randomly, e.g. they were asked about patients' motor skills such as their handedness or ability to drive a car. They could answer "Yes" or "No", or say that the patient sometimes did one thing and sometimes another, although the items referred to skills which normally remain constant. The responses of relatives and patients to these items were compared: no disagreement occurred and no respondent selected the nonsensical answer.

All respondents (patients *and* relatives) were first asked to describe the relative's coping strategies in their own words. Their answers were categorised by the interviewer according to which of the five styles they most resembled. Then the respondents were asked specifically whether each listed coping strategy had been used by the relative in the last three months.

Finally, each relative was given the Camberwell Family Interview, which was audio taped and then rated for Expressed Emotion (Vaughn & Leff, 1976*b*).

Results

Expressed Emotion

Fifteen of the relatives (54%) fell into the high-EE category as defined by Leff *et al* (1982). No significant relationship was found between high EE and the sex of the patient, the relationship between the patient and the relative, or whether the patient fell into the acute or chronic sub-group.

Hypothesis 1: Agreement within relative–patient pairs

The item-by-item agreement between relatives and patients was assessed using weighted kappa. Agreement over occurrence of problems and relatives' coping responses was generally low, ranging from 0.06 to 0.36, although significant agreement occurred on items referring to social withdrawal (problem occurrence, $P<0.05$; coping style, $P<0.03$), poor time-keeping (problem occurrence, $P<0.02$) and social skills difficulties (coping style, $P<0.01$). (The patients' responses to the filler items showed that they could cope with the demands of the task format, but it seems likely that their responses were unrealistic).

We concluded that patients did appraise the situation at home differently to their relatives, but that this divergence of views was not simply related to high EE: consequently Hypothesis 1 was not confirmed.

However, some suggestive findings do emerge from exploration of the data. Disagreements occurred as much because the patient considered that he had a particular problem which the relative denied as vice versa. The amount of warmth relatives expressed during the EE interview was (predictably) negatively correlated with the number of problems they reported (Spearman's $r=0.39$, $P<0.02$): warm relatives tended to report fewer problems than the patient and disagree more with the patient about the occurrence of individual problems. Thus warm relatives seemed to provide an accepting home atmosphere in which they denied the existence of problems, although the patients themselves were prepared to recognise that they did occur. The number of critical comments was not related to the number of problems that relatives identified. However, critical relatives tended to report more problems than the patient, and highly critical relatives achieved a significantly higher level of agreement with the patient than did uncritical relatives (Fisher's exact test, $P<0.02$).

Hypothesis 2: Unpredictability in relatives' behaviour

The relationship between relatives' reports of their coping responses and their EE ratings was examined. High EE as such was not significantly associated with the use of variable responses. However, high levels of EE can reflect either the number of critical comments or the degree of over-involvement; and as these ratings assess rather different types of behaviour, it is worth examining them separately.

There was a significant correlation in the expected direction (Spearman's $r=0.32$, $P<0.05$) between the number of critical comments and relatives' own ratings of the frequency with which they responded variably to problems: highly critical relatives tended to deal with problems in a variable or unpredictable fashion. On the other hand, no relationship was found between over-involvement and the tendency to use variable responses. Higher ratings of warmth were weakly associated with a tendency to use consistent, unvarying responses (Spearman's $r=0.26$, $P<0.10$). The patients' ratings of the frequency of variable responses were on average lower than the relatives' own estimates and were unrelated to any EE measure.

Thus Hypothesis 2 was confirmed in part: highly critical relatives (but not those who were over-involved) did appear to provide an unpredictable home environment.

Coping styles and EE

Relatives' tendencies to cope with problems in a warm, critical, or over-involved manner did not relate directly to their EE ratings. However, there was a predictably inverse relationship between the number of critical comments and the reported frequency of warm coping responses (Spearman's $r=-0.41$, $P<0.02$). Similarly, a negative relationship was found between the EE rating of warmth and the reported use of over-involved coping responses (Spearman's $r=0.39$, $P<0.02$). Thus relatives who relied on calm, accepting, caring means of dealing with problems were seldom critical, while those who responded anxiously and intrusively were rarely warm.

Acute and chronic cases compared

Using the standard cut-off point of 35 hours to define a high degree of contact (Vaughn & Leff, 1976*b*), a significant difference was found between the acute and chronic sub-groups (Table I): the relatives of chronic patients spent more time with them than the relatives of the more acutely ill patients. High-EE relatives tended to spend more time with their patients, but only the relationship between emotional over-involvement and the number of hours in contact was significant (Spearman's $r=0.42$, $P<0.01$); thus it seems to be the chronicity of the illness rather than the emotional quality of the relationship which determines the amount of time spent together. Variable responses to individual problems were significantly more common among the relatives of chronic patients (Table I). The relatives of the chronic sub-group also varied their coping style more from problem to problem (Table I): while six of the acute patients' relatives employed only one style across all ten problems, none of the chronic patients' relatives showed this degree of consistency.

Discussion

Our results suggest that some high-EE relatives do tend to provide an unpredictable environment for the schizophrenic patients with whom they live;

TABLE I

Acute and chronic patients compared, using Fisher's exact test

Aspect of patient–relative interaction	*Acute ($n=14$)*	*Chronic ($n=14$)*	*Acute vs chronic*
Hours of contact			$P<0.02$
High contact	4	10	
Low contact	10 (28%)	4 (74%)	
Use of variable responses			$P<0.05$
Rarely	11	6	
Often	3 (28%)	8 (57%)	
Consistency of relative's coping style			$P<0.01$
Consistent	6 (43%)	0	
Inconsistent	8	14	

although the only directly relevant correlation we found was between the second measure of unpredictability, based solely on relatives' variability of response, and one aspect of expressed emotion (number of critical comments). This unpredictable behaviour on the part of the relatives probably creates a cognitively confusing environment, of the kind liable to precipitate an exacerbation of the positive symptoms of schizophrenia. It is possible that relatives' coping styles mediate between their emotional attitudes and the exacerbation of symptoms in the patient, thus possibly explaining why patients living in high-EE homes are particularly prone to relapse. Alternatively, their coping styles could be a component of the constellation of behaviours and attitudes measured by the EE rating. This issue needs to be tested empirically.

Relatives and patients tended to have different perceptions of problems, although surprisingly the patients acknowledged the existence of problems just as frequently as their relatives did. Warm relatives tended to minimise difficulties, often identifying fewer problems than their patients. Highly critical relatives, on the other hand, consistently achieved a high level of agreement with their patients: it is possible that such relatives teach patients their own view of their difficulties. It thus appears that disagreement about day-to-day difficulties is not a factor contributing to relapse.

The differences between the acute and chronic sub-groups are intriguing. The prolonged effect of unpredictability in close relatives may be to maintain the chronically ill status of some patients; but it is equally possible that chronicity may induce unpredictability, as relatives try differing strategies to deal with intractable problems. Chronic patients were no more likely to come from high-EE homes or to have more problems, but they did spend more time in close contact with their relatives, who in turn were more likely to respond unpredictably to their behaviour. What is needed now is a longitudinal investigation of how the relative's coping style changes as the patient's behaviour changes with time and the condition becomes more chronic.

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*B. MacCarthy, BA, MSc, DipClinPsych, *Research Psychologist, MRC Social Psychiatry Unit, Institute of Psychiatry, De Crespigny Park, London SE5 8AF*

D. R. Hemsley, BA, MPhil, PhD, *Senior Lecturer, Institute of Psychiatry*

C. Shrank-Fernandez, BA, MPhil, *Locum Lecturer, Institute of Psychiatry*

L. Kuipers, BA, MSc, PhD, *Lecturer, Institute of Psychiatry*

R. Katz, BA, PhD, *Research Psychologist, Institute of Psychiatry*

*Correspondence

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Asperger's Syndrome and Tourette Syndrome:

The Case of the Pinball Wizard

We review the English-language literature on Asperger's syndrome (AS), with particular reference to diagnostic criteria and differentiation from infantile autism and personality disorders, and describe six cases seen in practice; all met DSM-III criteria for 'atypical pervasive developmental disorder'. Three also developed Tourette syndrome: the co-occurrence of the two disorders, and methods of intervention, are discussed.

Asperger's syndrome is a neuropsychiatric condition first described in 1944 by Hans Asperger, an Austrian physician. As a diagnostic classification it has been used for some time in continental Europe and more recently in the British psychiatric literature (Van Krevelen, 1971; Bosch, 1962; Isaev & Kagan, 1974), but it is not mentioned in DSM-III. A comprehensive review of the syndrome has been given by Wing (1981) and further work in the area is continuing. The question of whether the syndrome falls within the realm of developmental disabilities or of schizoid personality has been debated in the British literature (Wolff & Barlow, 1979; Chick *et al*, 1979; Wing, 1981). Indeed, some of the more recent work on criteria for personality disorder in the families of schizophrenics may describe patients with Asperger's syndrome (Kendler, 1984). We agree with Wing that the condition most properly falls within the category of autistic-like symptomatology—more specifically, 'pervasive developmental disorder'.

Patients with Asperger's syndrome (AS) characteristically present with developmental delay. Many, but not all, develop the syndrome from what appears to be an autistic stance in infancy. An earlier attempt to define the discrete differences between autism and AS was presented by Van Krevelen & Kuipers (1962). AS patients usually present with abnormal and often bizarre speech which is pedantic and aprosodic in quality. (Prosody refers to the rhythmic, inflective, tonal, and affective quality of spoken words, exclusive of the meaning of the words or phrases: aprosodic speech is speech without prosody, i.e. it is flat, atonal, emotionless and monotonous). Non-verbal communication is clumsy and is poorly co-ordinated with verbal utterances. Social interactions are characterised by withdrawal, interpersonal clumsiness, and a major deficit in empathy for others. Repetitive activities and resistance to change are often present. Stereotyped movements of the body and limbs occur occasionally. There is excellent rote memory, with hypertrophy of isolated interests and mastery of special interests. An increased incidence of mental retardation is observed but the condition is also consistent with normal intelligence. There is usually a discrepancy between verbal and performance IQ scores.

In a study of 35 000 children under 15 years of age in a specific geographical area, Wing & Gould (1979) noted six cases of Asperger's syndrome. The criteria they used for defining the syndrome included:

1. Pedantic, aprosodic, bizarre speech
2. Clumsy and uncoordinated non-verbal communication

3. Withdrawal or clumsy interpersonal relatedness
4. Defect in empathy for others
5. Repetitive activities
6. Resistance to change in activity or environment
7. Stereotyped bodily movement
8. Adequate-to-excellent rote memory
9. Circumscribed interest patterns

Asperger, Wing, and other authors have all agreed that the male:female ratio is quite high. In Wolff & Barlow's (1979) study the male:female ratio was 9:1, while Wing (1978) reported a ratio of 15:4 with classic symptoms and 13:2 among those who had many but not all of the features. Asperger's syndrome has been reported in identical triplets (Burgoine & Wing, 1983), but no other genetic investigations have apparently been undertaken.

A review of the English-speaking literature indicates that many authors feel that it is important to separate Asperger's syndrome from early infantile autism: both Asperger (1944) and Van Krevelen (1971) describe the AS population as being separable from the population of children we usually associate with autism. In our opinion most cases of Asperger's syndrome fall within the DSM-III category of 'pervasive developmental disorders', specifically 'atypical pervasive developmental disorder'. However, we believe that a specific sub-notation of 'Asperger-type' is applicable, as there may be important treatment implications which follow directly from that qualification.

The authors have had personal experience with six cases of Asperger's syndrome found in a population of 200 patients with 'autistic-like' symptomatology. All six met DSM-III criteria for 'atypical pervasive developmental disorder'.

Tourette syndrome is a neuropsychiatric disorder with onset between the ages of 2 and 15 years, characterised (according to DSM-III) by the presence of multiple motor tics and multiple phonic tics (occasionally presenting as coprolalia); the ability to suppress movements voluntarily for minutes or hours; a waxing and waning course; and a duration of more than one year. The condition often occurs concurrently with attention-deficit disorder and obsessive–compulsive symptomatology. Cases of Tourette syndrome with autism and with mental retardation have been described in the literature (Kerbeshian *et al*, 1984; Burd & Kerbeshian, 1985). Of our six patients with Asperger's syndrome, three also presented with Tourette syndrome: one of these cases is described in detail below. Data on all six patients is presented in Table I.

TABLE I

Characteristics of the six cases of Asperger's syndrome found in a population of 200 patients with 'autistic-like' symptomatology. Case DD is described more fully in the text

Case AA: 21-year-old male

(*a*) *Speech abnormalities:* Impaired prosody, monotonous speech, spasmodic utterance
(*b*) *Non-verbal communications:* Impaired
(*c*) *Social interaction:* Enjoys playing by himself, solitary at school
(*d*) *Repetitive activities:* Present
(*e*) *Circumscribed interests:* Computers; computer technology; mental telepathy
(*f*) *Tic symptoms:* Tourette syndrome
(*g*) *IQ:* Full scale 101
(*h*) *Response to medication (haloperidol):* None
(*i*) *Family history:* Alcoholism; depression; 'eccentric' uncle

Case BB: 12-year-old female

EEG: Normal
(*a*) *Speech abnormalities:* Spasmodic speech, whispered in quality
(*b*) *Non-verbal communication:* Impaired
(*c*) *Social interaction:* Isolation, poor peer relationships
(*d*) *Repetitive activities: data not available*
(*e*) *Circumscribed interests:* Hyperlexia; watching TV
(*f*) *Tic symptoms:* Tourette syndrome
(*g*) *IQ:* Verbal 104; Performance 71; Full scale 88
(*h*) *Response to medication (haloperidol):* Improved peer relationships, tics reduced, grooming improved
(*i*) *Family history:* Similar problem in brother; father an alcoholic

Case CC: 8-year-old male

(a) *Speech abnormalities:* Aprosodic, speech muffled
(b) *Non-verbal communication:* Very little; movement inhibited
(c) *Social interaction:* Plays by himself
(d) *Repetitive activities:* Repetitive reading, even though patient has a reading disability
(e) *Circumscribed interests:* Drawing; spends hours drawing elaborate diagrams
(f) *Tic symptoms:* Chronic vocal tic; no motor tics
(g) *IQ:* Verbal 91; Performance 118; Full scale 105
(h) *Response to medication (haloperidol):* Positive; affect improved; peer relationships improved
(i) *Family history:* Learning disabilities; mother with vocal tics

Case DD: 18-year-old male
EEG: Normal
(a) *Speech abnormalities:* Disturbance of prosody, rate and rhythms; speaks rapidly; high tonal pitch; very quiet
(b) *Non-verbal communications:* Very inhibited; little facial expression
(c) *Social interaction:* Limited; plays by himself; no friends; doesn't interact well with family or others
(d) *Repetitive activities:* Examines pieces of lint; draws complex pictures of pinball machines
(e) *Circumscribed interests:* Mathematics; computers; music
(f) *Tic symptoms:* Tourette syndrome
(g) *IQ:* Verbal 115; Performance 138; Full scale 129
(h) *Response to medications (haloperidol):* More open to other people, improved eye contact, feels calm, can plan activities now
(i) *Family history:* Non-contributory

Case EE: 11-year-old male
EEG: Normal
(a) *Speech abnormalities:* Poor prosody, mumbling
(b) *Non-verbal communication:* Very inhibited; flat facies
(c) *Social interaction:* Distant; plays by himself; doesn't interact well with significant others; poor peer relationships
(d) *Repetitive activities:* Drawing electronic diagrams
(e) *Circumscribed interests:* Electronics and energy; hyperlexia
(f) *Tic symptoms:* Stereotyped movement disorder; no tics
(g) *IQ:* Verbal 55; Performance 58; Full scale 52; felt to be low estimates
(h) *Response to medication:* Untreated
(i) *Family history:* Unknown

Case FF: 10-year-old male
(a) *Speech abnormalities:* Flat intonation; disjointed flow of information
(b) *Non-verbal communication:* Mechanical gestures out of synchrony with flow of speech; primarily unilateral gestures, alternating sides
(c) *Social interaction:* Socially clumsy; doesn't understand social norms; poor peer relationships
(d) *Repetitive activities:* Reading about radio and radio history
(e) *Circumscribed interests:* Talks about radio and radio programmes; tries to divert conversation to radio
(f) *Tic symptoms:* Stereotyped movement disorder; no tics
(g) *IQ:* Verbal 100; Performance 69; Full scale 84
(h) *Response to medication (methylphenidate):* Excellent response to methylphenidate for hyperactivity; other symptoms untreated
(i) *Family history:* Relatives with poor-eye contact, stereotyped movements, speech with poor prosody, over-activity; alcoholism; depression

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Case report

D.D. was originally seen at the age of 13. At that time he had difficulty in communicating with others, particularly adults. He was the second of two children, born after an uncomplicated full-term pregnancy, labour and delivery. Birth weight was approximately seven pounds. No neonatal problems were observed.

He sat unaided at the age of six months, crawled at eight months, and stood at eleven months. He walked at twelve months, dressed himself at three years, and was also riding a trike by the age of three. He could utter single words at 18 months and short phrases at two years, but sentences did not appear until the age of four, when he was enrolled in speech therapy.

He was a very visually-oriented person, highly interested in such things as pinball machines. He drew detailed pictures of pinball machines and had in fact made his own pinball machine. He spoke very little, did not relate well to adults, and did not have close friends. He had attempted to join the school basketball team, but would not take showers with the boys after practice because he did not like to expose himself.

An EEG was obtained and appeared normal. In the course of the mental status examination, the patient was distracted by various objects in the room, repetitively stroked his own body, engaged in manneristic movements of the hands and wrists, and would rhythmically pat himself. On one occasion he took a piece of fluff from the examiner's person, contemplated, it and then threw it away; during this action the examiner's foot was related to as an object rather than as being part of another person. No tic-like movements were noted. The patient's voice was high-pitched, monotonal, and stereotypic, with a machine-like quality.

The patient admitted to feelings of low self-esteem, but denied suicidal ideation. He also admitted to ritualistic and obsessive concerns such as compulsively drawing schemata for pinball machines. The impressions at that time was of schizoid personality or borderline personality in early adolescence. Although the patient's sense of reality appeared distorted by his compulsive and stereotypic relationship to the world of objects and people, his cognitive processing of interpersonal and physical events disclosed no breakdown in reality testing.

The patient was next seen at 18 years of age. His mother indicated that since he was last seen he had become obsessed with certain things, such as computers, and behaved in a 'goofy' fashion when something struck him as funny. He had inappropriate body movements and when nervous would pick up pieces of fluff and examine them carefully. In the past he had been put on tranquillisers, to which he responded by becoming a 'zombie'. He persisted in a number of oddities which made it difficult for him to relate to other persons. In particular he showed an extreme interest in computers and musical instruments. He had only marginal contact with his peers.

During the mental status evaluation the patient exhibited marginal personal hygiene: he was dressed in a dirty T-shirt and old jeans, and body odour was noticeable. Throughout the interview he avoided direct eye contact and when eye contact was made he would avert his gaze. He was restless, shifting his position often, and was distractible. He was often distracted by fluff on the floor, or by the texture of the chair. He engaged in multiple motor tics, which had started several years previously. These were primarily confined to the head, trunk and extremities. He would repeatedly flick his fingers and jerk his body. He also engaged in complex rituals which he stated helped him with his train of thought. These included repetitive movements of his fingers and wrist: they were in sequence and very rapid. His speech was frequently interrupted with an 'um' sound, and he appeared to have repetitive, stereotypic and spasmodic speech, with poor intonation. He frequently mumbled. Affect was dominated by anxiety. He denied blocking of thought, ideas of reference, ideas of influence, paranoid ideation, thought broadcasting, thought insertion, or hallucinations.

Motor and vocal tics have continued with a waxing and waning course over the years he has continued in treatment with us. Diagnosis was 'atypical pervasive developmental disorder', Asperger's syndrome and Tourette syndrome.

Discussion

It is the belief of the authors that Asperger's syndrome would be appropriately classified as a subgroup of the 'pervasive developmental disorders' delineated in DSM-III (American Psychiatric Association, 1980), since it involves severe deviations and delays along multiple lines of development and in a number of cognitive spheres. In AS one sees developmental delays and deviations in social interaction, speech and language development, non-verbal communication, and cognition. These give rise to areas of hypertrophied interest which may represent, on the one hand, obsessive–compulsive symptomatology, and on the other hand a form of adaptation in a person who is unable to relate to significant others but can relate to ideas or things. These traits are enduring within the individual and are characteristic of persons with the diagnosis of Asperger's syndrome. The wider term 'personality disorder' could therefore also be used to categorise the type of phenomenology present in these patients.

The course of development in our patients appeared to have given rise to the symptomatology of Asperger's syndrome by approximately the age of four. Subsequent development of Tourette syndrome followed in three cases, i.e. tic symptomatology was a secondary event. A fourth patient presented with tic symptoms but did not meet the criteria for Tourette syndrome. The patients with Tourette syndrome or other tic symptoms were treated with low doses of haloperidol, and in three out of the four cases improvement was observed not only in their Tourette and tic symptomatology but also in those symptoms specific for Asperger's syndrome; i.e. they related better to others, evidenced improvement in non-verbal communication and in their speech, appeared to be more outgoing, and fitted better into their cultural milieux. The patients without tics were not treated with haloperidol.

Pharmacological treatment is not the sole form of intervention available for Asperger's syndrome. One can hardly over-emphasise the importance of intensive psycho-educational intervention. Speech and language therapy with an emphasis on the prosodic features of speech may have a positive effect on outcome. Skill-training in the subtleties of social interaction, through rehearsal and practice, can also be of benefit. Exposure to social situations and set-up situations in which peers or significant others deliberately initiate interaction with patients is also very helpful. Unfortunately, the very factors which define Asperger's syndrome are negative indicators for insight-oriented psychotherapy. Moreover, insight-oriented psychotherapy has not proven to be of benefit in treating the symptoms of Tourette syndrome, and the literature on behavioural intervention with Tourette syndrome is inconclusive (Shapiro & Shapiro, 1981).

We know of no previous reports of the strong interrelationship between Asperger's syndrome and tic the disorders that appeared to exist among our patients. The developmental implications of this possible syndromic interrelationship are intriguing. We have seen an analogous interrelationship in four patients with DSM-III infantile autism who developed Tourette syndrome as a secondary feature. In those four, the development of Tourette syndrome was followed by an acceleration in development, i.e. the tic syndrome appeared to be a marker for improved outcome.

The degree to which Asperger's syndrome may represent a disorder of neurological development related to infantile autism is unclear. It has been hypothesised that Asperger's syndrome may be a milder form of infantile autism, with later onset. Our clinical experience tends to support the belief that the course of Asperger's syndrome is distinguishable from the usual course of infantile autism primarily by the crystallisation of the defining symptoms, the severity of symptoms, and the improved outcome. The age of emergence of AS is roughly four years; nonetheless many of these patients do exhibit abnormalities of motor development, ability to communicate and social development prior to the emergence of AS. The observed manifestations of this disorder appear to change in response to different developmental interactions between neuropsychiatric and environmental factors as the patients mature.

Of our six patients with Asperger's syndrome, three also developed Tourette syndrome and a fourth had a vocal tic. This high incidence of Tourette syndrome and other tics may reflect a referral bias, as individuals with tic disorders are referred to our clinic from all over the state, or alternatively may be due to tic symptomatology being misclassified under the description 'stereotyped movements' which has been frequently noted in previous descriptions of Asperger's syndrome. Given the small number of cases reported here, we can only speculate that the presence of Tourette and tic symptomatology in four of our patients with Asperger's syndrome represented a marker for a form of pervasive developmental disorder less severe than autism. The neurophysiology of such a marker is not clear. Further elucidation of the significance of these neurophysiological factors may be forthcoming as specific forms of pharmacological intervention are correlated with specific symptomatic responses. A useful area for further research would be to assess the response to haloperidol of Asperger's syndrome patients without Tourette or tic symptomatology. Such a study could be accomplished only with rigorous experimental design and with appropriate consent, given that haloperidol may cause tardive dyskinesia. Finally, there is an important need to refine specific psycho-educational treatment approaches to Asperger's syndrome and to ascertain if such programming can be enhanced by pharmacological treatment of selected patients. The authors are currently investigating this possibility.

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Jacob Kerbeshian, MD, *Associate Clinical Professor of Neuroscience, University of North Dakota School of Medicine, Grand Forks Clinic, 1000 Columbia Road South, Grand Forks, North Dakota 58202, U.S.A.*

*Larry Burd, MS, *Education Specialist, Child Evaluation and Treatment Program, Medical Center Rehabilitation Hospital, University of North Dakota, 1300 S. Columbia Road, Grand Forks, North Dakota 58202, U.S.A.*

*Correspondence

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Lithium Augmentation in the Treatment of Delusional Depression

Five patients suffering with delusional depression, and who were resistant to tricyclic antidepressants, were successfully treated with lithium carbonate. Delusional depression does not usually respond to tricyclic antidepressants, and ECT has been considered the treatment of choice. Such patients often refuse to acknowledge that they are ill. They, therefore, understandably often refuse to accept ECT. In order to treat, the Mental Health Act 1983 must be invoked. Treatment with lithium carbonate is more acceptable to most patients, and in the cases described, patients agreed to take this drug whereas they had refused to accept ECT.

Severe depressive illnesses may be accompanied by delusions of poverty, guilt, nihilism, and somatic change. Patients with such illnesses require admission to hospital and generally show poor response to tricyclic antidepressants: Charney & Nelson (1981) reported only a 22% response rate compared to 80% in non-delusional depression.

Slater & Roth (1969) observed that, in their experience, persistent delusional depression requires treatment with ECT. In their double-blind ECT study, the Northwick Park team (Crow *et al*, 1984) found that depressive delusions were the best targets for ECT. Glassman *et al* (1975) have also advocated the use of ECT in preference to tricyclics, as tricyclics alone may well prolong suffering.

The advantages of a combination of tricyclics and phenothiazines have been demonstrated by Nelson & Bowers (1978) in a retrospective study; and Spiker *et al* (1982) have published a preliminary report of a prospective double-blind study demonstrating a 79% response rate to this combination of drugs. Price *et al* (1983) have suggested that combined neuroleptic–tricyclic treatment of depression should be augmented with lithium. In refractory cases of depression, augmentation of tricyclics with lithium has been reported as resulting in a rapid resolution of symptoms: de Montigny *et al* (1983) claimed to have seen improvement within 48 hours, while Henninger *et al* (1983) observed that one-third of their refractory depressives improved within six days.

Our experience suggests that depressive delusions often respond to a combination of tricyclic antidepressants and lithium, and that the use of lithium may obviate the use of ECT in cases which are traditionally thought to be resistant to drug treatment alone. In support of this suggestion we describe briefly in this paper five patients with depressive delusions who had refused to give consent for electroconvulsive treatment and were then successfully treated without it.

Case Reports

The patients described below were all treated with lithium carbonate, lithium levels being maintained between 0.5

and 1.0 mmol/litre. Renal function and thyroid function studies were carried out prior to treatment.

Case 1

Mrs O.S., aged 38, was admitted with a relapse of depression, the fourth episode in ten years. She said: 'My hair is changing colour. My teeth are growing big. I am ugly'. She was mildly agitated.

In the past she had harboured similar somatic delusions on two occasions, but had responded to ECT. On both these occasions she had had periods of hyperactivity lasting 2–3 weeks. Her maternal aunt also had a history of depressive illness.

Her general practitioner started treatment with amitriptyline at a dosage of 150 mg a day, but after four weeks she was still agitated, and overtly deluded. She was admitted to hospital and was recommended ECT, which she refused. Treatment with lithium was started, and there was a dramatic improvement within 24 hours. However, the patient erroneously assumed that it was 'sleeping tablets' that were being prescribed, and failed to take them the next day, only to deteriorate on the third day. When this was discovered, treatment with lithium carbonate was restarted, and resulted in dissipation of her symptoms within 24 hours. She was still well at follow-up 3 months later, and then stopped attending the out-patient department.

Case 2

Mrs E.E., 59 years old, had had her first episode of depression two years earlier. She was treated initially by her general practitioner with dothiepin (150 mg a day) and later with ECT, to which she responded. In spite of continued dothiepin (150 mg a day) she relapsed some months later. She stated: 'My brother has manic–depressive psychosis and it's all because of me. I'm lousy, I did it all'. She was advised to have further ECT but refused. Treatment with lithium started on the sixth day after admission, and after two weeks she stopped discussing the possibility of her causative role in her brother's illness. She was discharged two weeks later. She has continued to attend the out-patient clinic, and is still well after 12 months.

Case 3

Mr H.D., a 72 year-old pensioner, presented himself as being in abject poverty: 'I have bought a new car, and this has made me poor. I have ruined my family name. I have lost all my money. My wife and I cannot live on our pension now.'

He had suffered a depressive illness about 20 years earlier. Hospital case notes of the time revealed that he had severe guilt feelings about his adolescent adventures with his girlfriends, and was harbouring suicidal ideas. He did not report to work for over six months. He improved with mitriptyline (200 mg a day), Stelazine (15 mg a day) and benztropine (6 mg a day), but as the drugs were gradually reduced he relapsed. He was then given eight ECTs and after that had stayed well until his present illness.

His brother had also had a depressive illness in the past, and had responded to treatment with amitriptyline and ECT. His father had mysteriously fallen off a bus and died at the age of 74: it was not clearly established whether his death was accidental, as he was reported to have been despondent before the incident.

Out-patient treatment with amitriptyline was started, but Mr H.D. did not improve. Increasing the dose of amitriptyline led to severe side-effects, including retention of urine. The patient was then admitted and ECT was recommended, which he refused. Treatment with lithium carbonate was introduced, supplementing a lower dosage of amitriptyline. The patient improved within a week, and continued with the combined treatment as an out-patient. Medication with lithium carbonate was stopped after six months, and Mr H. D. remains well after one year.

Case 4

When presenting to a psychiatrist for the first time, Mr J. F. (aged 64) was markedly agitated and had not slept for a week prior to the consultation. His medication when seen was dothiepin, 150 mg per day. He believed that he was dead; 'The world has ended, I don't need to eat.'

His wife informed us that he had probably had a self-limiting episode of depression at the age of 21. They had not then been married, but she was told that he had not reported for work for about two months, and slept very badly. This episode had not been documented.

At the initial consultation he was invited to enter hospital, which he did, but refused to undergo ECT. He was maintained on dothiepin 150 mg a day and lithium was added to his medication. At the end of two weeks he functioned effectively, ate and slept well, and seemed to be quite cheerful. Treatment with lithium was continued on an out-patient basis for a year, and then stopped. He was still well 6 months later.

Case 5

Mr R. F., aged 69, had suffered from Parkinson's disease for nine years. He had taken premature retirement when he could not cope with the adolescents to whom he had taught music for over 15 years; then a home improvement grant which he had been promised fell through. The couple decided to draw on their savings, and he felt that they had been 'reduced to paupers.' He was preocuppied with his weekly food bills, and became very agitated.

He had been prescribed procyclidine (5 mg a day) for the last nine years. For the depression, his general practitioner started him on mianserin, 150 mg a day. As there was no improvement a psychiatric opinion was obtained, and after four weeks Mr R. F. was admitted to hospital. The dose of procyclidine was increased to 5 mg twice a day, but he developed urinary retention and severe constipation. He was therefore switched to carbidopa (110 mg twice a day) and was also offered ECT, which he refused. He was then given lithium carbonate. After two weeks his activity levels increased, and after remaining in hospital for about a month he was well enough for discharge. His wife later reported that he was 'almost his old self now.' He still has Parkinsonian features, but they are less in evidence, and his agitation, especially over money matters, has been completely relieved. He is continuing to take lithium carbonate, and remains well six months after discharge.

Discussion

Depressed patients with delusions have been found to be unresponsive to tricyclic antidepressants. By the very nature of their symptoms, such patients may not consider themselves to be ill, and so may not agree to ECT; but if this is regarded as the treatment of choice they can be detained under the Mental Health Act (1983), although a second opinion has to be obtained (via the Mental Health Act Commission) before electro-convulsive treatment can be commenced.

Four of our patients had previously suffered a depressive illness. One had recovered without treatment; three had improved after ECT (two of these had also been prescribed psychotropic medication). All five patients refused ECT for their current episode of depression.

To test the hypothesis that lithium augmentation of antidepressant medication is effective as a treatment for delusional depression, it would be appropriate to carry out a double-blind trial. However, patients with delusional depression are relatively rare. Furthermore, because they blame themselves for their current situation and do not fully accept that they are ill, they could not give informed consent to a research trial involving a double-blind treatment regime. In Case 1 (described above), the patient stopped taking lithium and her condition deteriorated within 24 hours. This discontinuation of treatment was, in a sense, double-blind: the patient was mistaken as to the nature of the drug and her doctor (AW) was not aware of her non-compliance. When lithium was re-started the patient once again improved within 24 hours, and remained well as treatment continued.

We can thus point to the resolution of delusions and elevation of depressed mood in five cases which were refractory to normally therapeutic doses of antidepressants (tricyclics were tried in four cases, mianserin in the other). We suggest that lithium in combination with an antidepressant is an effective treatment for delusional depression, and is more acceptable than ECT to many patients.

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M. Pai, MD, DPM(Bombay), *Registrar, Charles Burns Clinic, Moseley, Birmingham*

*A. C. White, MD, MRCPsych, *Consultant Psychiatrist, The Queen Elizabeth Hospital, Queen Elizabeth Medical Centre, Edgbaston, Birmingham B15 2TH*

A. G. Deane MRCPsych. *Senior Registrar, Midland Nerve Hospital, Birmingham*

*Correspondence

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Locus of Control in Short and Long Sleepers

ANAND KUMAR and A. K. VAIDYA

Behavioural scientists are currently attempting to correlate individuals' usual duration of sleep with personality traits as well as with personality profiles. Studies using the Minnesota Multiphasic Personality Inventory (MMPI) and Cornell Medical Index have suggested that differences between "short sleepers" and "long sleepers" show up in such traits as self-control, anxiety, extroversion, aggression and ambition (Hartmann *et al*, 1972; Spinweber & Hartmann, 1976), although Webb & Friel (1970, 1971) found no such differences. Glaubmann & Orbach (1977) observed short sleepers to be efficient, energetic, ambitious, self-content and socially well adjusted.

In a study by Hicks & Pellegrini (1977) the 17 longest and 17 shortest sleepers were selected from 300 college students: only those individuals were included who reported that they had experienced the same sleep duration for at least the preceding six months. It was found that the short sleepers had significantly higher anxiety scores on the Taylor Manifest Anxiety Scale than the long sleepers. By contrast, Hartmann (1973) saw short sleepers as "non-worriers".

Kumar & Vaidya (1982a) reported higher neuroticism in short sleepers than in long sleepers; and according to Eysenck & Eysenck (1975) neuroticism is similar to anxiety, so that a high score on neuroticism indicates anxiety and worry. Stuss & Broughton (1978) found short sleepers to show high levels of activity and regressive tendencies and to give an outward appearance of good adjustment, but Kumar & Vaidya (1982b) reported significantly *poorer* adjustment among short sleepers than among long sleepers. In a recent study by Kumar & Vaidya (1984), 25 short and 25 long sleepers were tested on the Sinha Anxiety Scale (Sinha, 1968) and a significantly higher mean score was found for the short sleepers.

This study seeks to examine the relation, if any, between the sleep patterns of consistently short and long sleepers and their individual perceived locus of control. Locus of control is a personality dimension, developed by Rotter (1966) from social learning theory, which describes the degree to which an individual believes that reinforcements are contingent upon his own behaviour. According to Lefcourt (1966), people with an internal orientation tend to see the things that happen to them as being due to their own actions; that is, they see themselves as responsible for what happens to them. People with an external orientation tend to see the things that happen to them as being unrelated to their own actions: they are perceived as being due to factors beyond their control (powerful others, luck, fate, etc.) Research into perceived internal versus external control of reinforcement as a personality dimension is expanding rapidly.

Method

Following the method of Hicks & Pellegrini (1977), we asked 500 male college students "How many hours do you sleep each night?", and on the basis of their replies selected the 50 who slept least and the 50 who slept most. Individuals were included only if they reported that they had experienced the same duration of sleep for at least the preceding year and were satisfied with that amount of sleep. The ages of those selected ranged from 18 to 28, with a mean of 24.82 years.

To measure the extent to which each subject perceived reinforcement as contingent upon his own action, we used a Hindi version (Kumar & Srivastava, 1983) of Rotter's Locus of Control Scale (Rotter, 1966). This scale is a 29-item forced-choice test, scored so that high scores indicate an expectancy of external control of reinforcement and low scores indicate an expectancy of internal control. Six filler items are also included in the scale to disguise the purpose of the test.

Results

The long sleepers had higher scores on the Locus Control Scale (mean 12.28, s.d. 2.38) than the short sleepers (mean 10.76, s.d. 2.50). Comparison of these means showed that the short sleepers were significantly more internally controlled than the long sleepers ($t=3.40$; d.f.$=98$, $P<0.01$).

Discussion

The finding of the present study should be interpreted in the context of Rotter's social learning theory, when it may be concluded that short sleepers, being internally controlled, perceived reinforcements as contingent upon their own action and are more active in their attempts to master and change their environment, while long sleepers are externally controlled and are fatalistic about their experiences. These results are contrary to the conclusion of Webb (1979) that there are no personality differences between short and long sleepers.

Sleep abnormalities are common among psychiatric patients, which our subjects were not. Nor should the short sleepers of this study be confused with complainers: our results would not inevitably apply to a clinical population of patients who complained of insomnia. Our subjects were content with little sleep.

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*Dr Anand Kumar, FWASP, *Lecturer, Department of Psychology, Kashi Vidyapith University, Varanasi 221002, India*

Dr A. K. Vaidya, *Lecturer, Department of Psychology, Kashi Vidyapith University*

*Correspondence

(*Accepted 20 May 1985*)

British Journal of Psychiatry (1986) **148**, 741

Correspondence

Schizophrenia with Good and Poor Outcome

SIR: The letter by Drs Nimgaonkar & Murray (*Journal*, March 1986, **148**, 343–344) misrepresents some aspects of our studies (*Journal*, March and April 1985, **146**, 229–246 and 348–357). According to the opening and closing sentences of their letter, these studies illustrate the difficulty of obtaining longitudinal information from a cross-sectional study, and the design allowed us to do no more than confirm what is already known about the prognostic significance of certain clinical features. These comments may suggest (misleadingly) that the principal aim of our investigation was to find clinical predictors of outcome in schizophrenia. In fact, it was concerned mainly with 'cross-sectional' questions: whether patients with persisting schizophrenic symptoms also show signs indicating organic brain dysfunction (an abnormal CT scan, neurological soft signs and/or cognitive impairment); whether these 'organic' signs are inter-related; and whether they are associated with any particular chronic psychiatric symptoms. The 'longitudinal' information, imperfect because obtained retrospectively, was reported to indicate whether the groups with good and poor outcome differed in the early stages of illness, especially in the quality of remission and response to neuroleptics at that time.

The possibility that some of the 'organic' abnormalities may have been "... consequent upon poor outcome or factors associated with it ...", was not ignored but discussed at some length in the second and third papers in the series. Though these papers presented in detail the abnormalities found and included tentative interpretations, they were somehow disregarded in the letter. Further, we have not claimed that our data "have eliminated all likelihood of pharmacological tolerance" in patients who respond unsatisfactorily to treatment with neuroleptics. We have only said that our data on drug bioavailability and prolactin response provided no evidence for such tolerance.

Finally, though our sample was not representative for the prevalence of particular types of outcome, it included the full range of outcome states, from asymptomatic remission to chronic psychosis. Drs Nimgaonkar and Murray comment disapprovingly that the non-representative character of the sample did not deter us from "making the sweeping generalisations about possible sub-types of schizophrenia". In fact, our "sweeping generalisations" consisted only in supporting the distinction between sub-types with good and poor outcome—a distinction which under various names has been discussed for at least half a century.

TAMARA KOLAKOWSKA
Department of Psychiatry Research Unit
Oxford University
Littlemore Hospital
Oxford OX4 4XN

Expressed Emotion and Relapse in Schizophrenia

SIR: In their letter (*Journal*, February 1986, **148**, 215) about our recent paper on expressed emotion (EE) and relapse in schizophrenia (MacMillan *et al*, 1986*a*), Drs Leff and Vaughn are apparently undecided whether our results are an inappropriately interpreted replication of their own work or are flawed by fundamental methodological defects. We wish to clarify some of the issues involved.

The chi-squared analysis used by Leff & Vaughn to give a positive interpretation of our results ignores the confounding effects of treatment and duration of illness preceding admission, and makes inefficient use of available data on time to relapse (Peto *et al*, 1977). Moreover, it is incorrect to exclude even the small numbers of patients lost to follow-up in this study. In dismissing the influence of treatment status Leff and Vaughn make the customary error (Altman,

TABLE I.

	Active	*Placebo*	*Total*
Low EE	14	10	24
High EE	9	18	27
Total	23	28	51

$\chi^2 = 3{\cdot}21$, d.f. = 1, $P > 0.05$.
Low EE: odds on Active treatment: $\frac{14}{24}/\frac{10}{24} = 1{\cdot}4$.
High EE: odds on Active treatment: $\frac{9}{27}/\frac{18}{27} = 0.5$.

1984) of assuming that lack of significance at $P = 0.05$ implies absence of association. This may be illustrated by the data relating to EE and treatment status (Table I).

Here χ^2 is non significant at $P = 0.05$, but the odds on active treatment in the low EE group are 1.4 compared with 0.5 in the high EE group, giving an odds ratio of 2.8 (with 95% confidence limits at 0.78 and 10.4). The conclusion that there is *no* association between EE status and medication is therefore not supported by these data.

Leff & Vaughn make two main methodological points—that relatives may have been misclassified with respect to EE status, and that our definition of relapse/readmission is unsatisfactory.

Since the inception of EE research over 20 years ago, whatever convention has been used, the procedure adopted has been modified in the face of the exigencies of the practical situation (e.g. Brown *et al*, 1962; Vaughn & Leff, 1976; Vaughn *et al*, 1984). Table II shows the nature of the home and the identification of the key relative in our study. For those living in marital homes there appears to be no problem. In non-marital homes we attempted to adopt the original convention of Brown *et al* (1962) of identifying the key relative as "the most closely

TABLE II.
Nature of homes and identification of key relatives for EE sample

Nature of home	*Number of patients*	*Key relatives*	*Details of key relatives, including reason for their closer contact*
Marital home	17	4 wives 12 husbands 1 cohabitee (female)	
Parental home			
Single parent	23	5 fathers	1 divorced; 4 widowed
		18 mothers	9 divorced; 6 separated; 3 widowed
Both parents	38	3 fathers	1 retired father, mother working abroad; 1 mother avoiding patient (aggression); 1 mother frail and saw little of patient, also refused visit
		28 mothers	5 fathers generally absent from home (e.g. seafaring); 1 father severe alcohol problem and rarely sober; 12 fathers in full-time employment, mothers not employed; 2 children of patients in home and mother had close contact; 8 cases no special reason for mother's closer contact
		6 mothers and fathers seen. Mother key relative	1 both retired; 4 both working (in 3 cases in identical jobs); 1 mother physically unwell, father works but often home
		1 sister-in-law	Total adult family members 11, and sister-in-law closest contact
Sibling home	4	1 brother	Only sibling present
		3 sisters	1 only sibling present; 1 married sister (spouse often absent through work); 1 adult sister, school-aged brother in home

related female living in the household—typically a wife or mother. Obvious exceptions were made in cases in which patients lived only with a male relative". We did however take note of the extent of the contact between family members and the patient. Although in most cases contact was greatest with the key relative identified as above this was not always so. Sometimes, for a variety of reasons (Table II), there was much more contact with another relative and where this was so that person was identified as the key relative.

Twenty three of the 61 cases living in parental homes lived with single parents. The mother only was seen in 28 cases where the patient lived with both parents and clearly spent more time with the mother. In three cases the mother was not interviewed. One mother worked as a housekeeper for a middle-Eastern family and was often abroad while the retired father spent much of his time at home. Another mother was in frail health and declined interview, although her husband (who spent more time with the daughter) was willing. In the third case the son was aggressive, and it had been decided in the family that the father would deal with him while the mother saw little of him. In six cases the extent of the contact with the relatives was unclear and both parents agreed to be interviewed. The final case concerned an itinerant family comprising eleven adults and numerous children living in 3 caravans. The father was generally absent from home. The mother, nursing a neonate, did not live in the same caravan as the patient. The patient shared a caravan with her brother's wife and therefore this sister-in-law was considered the key relative in this case. Four patients lived with siblings who were all considered as key relatives. Our analysis included every patient whose relative(s) were rated for EE so as not to introduce selection bias by exclusion. In this multicentre study of first episode cases it would not have been possible to gain the co-operation of all 308 adult relatives who could have been considered for interview. The heterogeneity of the family circumstances (Table II) illustrates some of the difficulties in assessing EE according to Leff & Vaughn's current recommendations.

Leff & Vaughn's second methodological objection is to our definition of relapse. In a multicentre trial it is necessary to adopt a broad definition. It is however clear from Crow *et al* (1986) that in 59 of 66 cases relapse was associated with the development of psychotic features. In the trial-eligible cases readmission was considered as equivalent to relapse as defined in the trial protocol. The closeness of this parallel is illustrated in Figure 1 in MacMillan *et al*, 1986*b*. We note that in their own studies Leff *et al* (1982) write that "an independent rater, Dr Paul Bebbington, was recruited to make the assessments blindly. He did not always concur with the view of the patient's clinician that a relapse had occurred."

Leff & Vaughn comment on the high proportion of immigrants in our sample excluded from our study of EE on the basis that they were of unassimilated immigrant background. Such patients either had relatives whose English was too limited for meaningful communication or lived in family circumstances which were not analogous to those of western culture. Leff & Vaughn's statement in the last paragraph of their letter that EE techniques are applicable to the Hindi-speaking is of interest but of little relevance to the present study. It is clearly impossible to include in such work persons who do not share a common language with the investigators. In spite of the advantage of a trilingual interviewer (AG) some exlusions had to be made.

Returning to the central issue of interpretation, the data in Table IV of our Paper (MacMillan *et al*, 1986*a*) have been used by Leff & Vaughn to estimate a crude relapse rate of 86% by 2 years in the high-EE group allocated to active treatment. The actuarial estimate is 71% (with 95% confidence limits at 38% and 100%). These confidence limits made it clear that these results must be interpreted with caution. We cannot agree that our views expressed in MacMillan *et al* (1986*a*) are inappropriately negative. We believe that Leff & Vaughn's consistently optimistic interpretation of the EE hypothesis rests upon an erroneous analysis of our own findings and an ability to ignore a number of problems which are now apparent in this literature.

Finally, we have two regrets. Firstly, it seems unfortunate that the involvement of Drs Leff & Vaughn in the editorial assessment (their letter appears in the same issue as our paper) did not lead them to forward their criticisms, at least of our bibliography, to us as part of the review process. Secondly, we are sorry that the findings, or our interpretation of them, have been less than welcome to colleagues whose assistance in initiating this project was much appreciated.

J. F. MacMillan
A. Gold
T. J. Crow
A. L. Johnson
E. C. Johnstone

Clinical Research Centre
Watford Road
Harrow, Middlesex HA1 3UJ

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Criteria for Measuring Change: Statistical Significance vs Clinical Significance

SIR: Eccleston *et al* (*Journal*, December 1985, **147**, 623–630), in their double-blind comparison of propranolol with thioridazine, conclude that propranolol resulted in a significant improvement on both the BPRS and the NOSIE, suggesting that it is useful in the treatment of chronic schizophrenia. Propranolol had a significant influence on both positive and negative symptoms of schizophrenia. In contrast, thioridazine had little to offer this group of patients. Their criteria for measuring the efficacy of propranolol does produce few statistically significant results. The central issue in a study such as this one is whether a statistically significant finding is also clinically significant or meaningful?

In using a maximum dose of 400 mg thioridazine per day, there seems to be an assumption that this is an adequate dose for treating schizophrenic patients. Davis & Garver (1978) have summarised the results of 207 double-blind comparisons of neuroleptics with placebo. There were 66 comparisons of chlorpromazine with placebo, and in 11 studies which did not show a significant treatment effect for chlorpromazine the dosage was inadequate. Chlorpromazine proved superior to placebo in all studies using daily doses of 500 mg or more. The relative potency of thioridazine is more or less equal to chlorpromazine (Davis, 1974). It may, therefore, be argued that the failure to get a treatment effect for thioridazine is because the investigators used a sub-optimal dose of the drug. Since all the patients recruited into the trial were already on neuroleptic medication and yet had florid psychotic symptoms, it would be of interest to document if the mean dose prior to commencing the trial was higher than 400 mg of thioridazine or its equivalent. For a sounder methodology, as well as to do justice to thioridazine, one should use a dose higher than that the patient was on prior to the trial. That is likely to alter the clinical effect of thioridazine as well as the statistical significance for the change in ratings, and perhaps also affect the between-group differences. Understandably, the investigators must have had good reasons for using this dose and drug (e.g. for blindness of the study). Theoretically, the inclusion of a placebo control group would have made it possible to conclude whether the patient population was treatment-responsive or not and thus account for the failure of response to thioridazine.

It is not clear if Eccleston *et al* found a between-group significant difference on the BPRS. The paper refers to propranolol resulting in a higher fall from base-line than thioridazine, but since the time period is not specified it perhaps refers to day 14 or 21 rather than to a significant effect throughout or at the end of the trial period. Patients in the propranolol group were also more severely ill at base-line, compared with the thioridazine group, and so there was greater room for change. The significant change in score reported in the propranolol group is, therefore, a weak effect. It is difficult to comprehend how a change from a mean base-line score of 24 to 16 on day 14 is significant at the level of $P<0.001$, whereas a reduction from a mean base-line level of 24 to approximately 15.5 on day 21 is significant at the level of $P<0.01$. What appears to be a marked improvement is an illusion (as can be seen if the Figure is redrawn by completing the broken line for mean BRPS score), since the maximum reduction in score is of the extent of only 33%. After day 21 the initial effect is dissipated. Thus a statistically significant result is probably not clinically significant, as considerable psychopathology is still evident at the end of the trial.

In our recent study (Manchanda & Hirsch, 1986) comparing d-propranolol with placebo with all the patients receiving haloperidol during the first week, we observed that d-propranolol had a better effect than placebo in sustaining the initial improvement with haloperidol. The overall magnitude of clinical change from pre-treatment scores was small, the majority of the patients showing little or no overall improvement. We concluded that although d-propranolol has a detectable therapeutic effect on schizophrenic symptomatology, this effect is more of pharmacological interest than of major clinical significance, as the change on rating scales did not compare favourably with the changes observed with conventional neuroleptics in adequate doses.

Propranolol has been a subject of research for over a decade, and several studies conclude that it has a statistically significant effect in reducing psychotic symptomatology. Clinicians are far from convinced. A weak antipsychotic effect for propranolol is the best that can be concluded from experience so far. It remains to be seen whether or not the propranolol molecule can be modified to produce a more effective antipsychotic agent. The clinical investigator has done his work and this is now a challenge for the pharmaceutical industry.

RAHUL MANCHANDA

University of Western Ontario
St Thomas Psychiatric Hospital
St Thomas, Ontario, Canada N5P 3V9

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MANCHANDA, R. & HIRSCH, S. R. (1986) Does propranolol have an antipsychotic effect: a placebo controlled study in acute schizophrenia. *British Journal of Psychiatry* (in press).

Professor Eccleston and Dr Hassanyeh Reply

SIR: Dr Manchanda asks if a statistically significant finding should also be seen as clinically significant. He concludes that with propranolol in schizophrenia (despite several studies which suggest a useful contribution) clinicians would regard such a finding, based on statistical significance, unconvincing. It is axiomatic that progress in research must be based on scientific methodology including statistics. If we revert to clinical opinion only, little progress in psychiatry can be hoped for. This, of course, does not mean that the findings of a study must be seen as clinically binding.

Dr Manchanda asks whether a dose of 400 mg thioridazine was therapeutically adequate. This is a relevant question, and further studies exploring this are obviously required. Our study, however, clearly suggests that propranolol at a dose of 640 mg a day was superior to thioridazine at a dose of 400 mg a day in patients with chronic schizophrenia. This superiority is based on the statistical findings in relation to measures on the BPRS (total score, positive and negative symptoms) and on the NOSIE. It should be noted also that although the improvement was not large there was a variation between the patients, some doing much better than others—but not in such a way that one could predict who was likely to show most benefit.

We do not suggest that propranolol radically changed or cured the illness—tables III and IV of our paper attest to that. What we do suggest is that it reduced the severity of some of the positive and negative symptoms; i.e. it made a quantitative and not a qualitative impact on the illness. Our conclusions were that propranolol at 640 mg/day may have a useful part to play in the treatment of chronic schizophrenia but that thioridazine at 400 mg/day does not. We also suggested that propranolol's effects on the negative symptoms warranted further investigation.

Would a higher dose of thioridazine have been more efficacious? As indicated earlier, this needs to be tested out in a clinical trial. Our impressions, however, are that it would not. Pre-trial, virtually all patients, whether in the propranolol or thioridazine group, were on *both* a depot and an oral neuroleptic at doses which clinicians would not have regarded as sub-optimal, yet despite which their illness had shown little or no change. If in this group of patients propranolol was shown to be beneficial, as was shown in our study (if only in a quantitative sense), what we suggested was that it ought at least to merit consideration in the drugs available to us which could be used in this condition.

DONALD ECCLESTON
FUAD HASSANYEH

The Royal Victoria Infirmary
Queen Victoria Road
Newcastle upon Tyne NE1 4LP

Is there a Right-hemisphere Dysfunction in Asperger's Syndrome?

SIR: We read with interest the report on a case of Asperger's syndrome (*Journal*, November 1985, **147**, 566–509), an entity unknown to us. We were surprised to see that one of the main features was non-verbal communication disorder (the inability to perceive the meaning of expressions and gestures of others and a poverty of non-verbal expressions), which has been named global aprosodia by Ross (1981) and is caused by right-hemisphere damage. The discrepancy between verbal and performance IQ in this patient also suggests right-hemisphere damage, as the authors pointed out. Wing (1981) reviewed six cases of Asperger's syndrome. Five of her six patients did the WAIS or WISC tests; in four of them the verbal IQ was higher than the performance IQ (being quite a bit higher in two of them).

Weintraub & Mesulam (1983) described 14 patients with right-hemisphere dysfunctions; as Denckla (1983) points out, they resembled those with Asperger's syndrome. The Weintraub & Mesulam patients had five features (introversion, poor social perception, chronic emotional difficulties, inability to display affect, and impairment of visuospatial representation); Asperger's syndrome patients show four of these (Wing, 1981).

Weintraub & Mesulam (1983) found a history of neurological disorders (infantile hemiplegia, perinatal stress and seizures) in 10 patients, and three of the remaining four had an abnormal family history. Wing (1981) described a history of cerebral damage in some patients, and found that parents' behaviour often resembled their childrens'.

These facts suggest that both groups of patients, those with Asperger's syndrome and those of Weintraub & Mesulam, are rather similar or share some characteristics. Perhaps the problem is inadequate communication between neurology and psychiatry. Weintraub & Mesulam emphasize right-hemisphere dysfunction but interpersonal aspects are stressed in Asperger's syndrome.

J. de Leon Molina

C. E. Ramon y Cajal
Madrid, Spain

J. Muñoz Ruata
E. Pico Soler

C. E. V. de Lourdes
Majadahonda, Spain

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Depression in General Practice

Sir: In their valuable study of the clinical features of depression in general practice and comparison with out-patients, Sireling *et al* (*Journal*, August 1985, **147**, 113–119) state: "Important factors associated with psychiatric referral appear to be severity and chronicity of the depression. This contrasts with Fahy's findings that neither factor played a major part, although both might be expected to do so".

Neither of these statements is completely accurate. First, Sireling *et al* (1985) did not study the psychiatric referral process. They compared general practice (GP) depressives (recognised and not recognised, etc.) with a separate group of depressed out-patients. This procedure does not justify conclusions—however correct these may later turn out to be—about factors affecting the process of referral. Secondly, my study (Fahy, 1974) was a prospective study of GP-identified depressives specifically designed to show how referrals differed from non-referred depressives from amongst a defined general practice population at risk. Subsequent reports of the findings made it clear that by every usual criterion of severity of illness (rating scales, weight of symptoms, factor scores, etc.) referred depressives were more severely ill and more endogenous. However, Sireling *et al* appear to have been misled by one set of multiple regression data (Table II in the paper in question) which showed that 'severity' and 'duration over one year' were statistically outweighed as predictors of referral by five other features, notably 'hopeless'. They appear not to have noticed that 'severity' was rated not by the research psychiatrist but by the eight collaborating GPs whose reliability was not measured.

The failure of these two features to emerge as superior predictors of referral does not mean they are of no value for this purpose in practice. The arithmetic of regression analysis assigns a weight to each variable expressing the individual predictive power of that variable when relationships with all other variables have been taken into account. The relatively minor roles of 'severity' and 'duration over one year' mean that it is unnecessary to invoke these variables in prediction of referral because of the greater importance of other clinical features which are themselves correlated with either severity or chronicity or both. In fact, the combined predictive power for referral of both 'severity' and 'duration over one year' was 14.4% of the total predictive value of the eight features considered in this particular analysis. Far from being "in contrast" with my data, Sireling *et al's* observations in this context are quite consistent with mine despite differences in material and method and an interval of more than ten years between the two studies.

Concepts of severity and of chronicity are difficult to define precisely in community settings. Total rating scale scores, symptom counts, weighted scores on dimensions, time off work etc. are just some of the influences contributing to severity ratings in general practice. It is apparent from the comparative work on GP versus hospital depression now appearing that although the statistical significance of differences is impressive, the magnitude of these differences is often quite small.

T. J. FAHY

Department of Psychiatry
University College
Galway

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The Nottingham ECT Study: Double-Blind?

SIR: Gregory *et al* (*Journal*, May 1985, **146**, 520–524) state: "The rater and clinical teams in charge of patients were blind to the treatment group." The statement that a trial is "double-blind" does not make it so. The authors are not seen to attempt to disprove their "double-blind" design by assessing blindness in the rater, the clinical teams and the patients at every assessment point, when a lack of blindness would influence results. Notionally blind participants can be asked to guess patient status and then the observed guesses can be compared with guesses to be expected by chance, thereby quantifying any disparity between theory and practice using conventional statistical criteria. If it is believed that simulated, unilateral and bilateral ECT produce different degrees of dysmnesia then these could vitiate the "double-blind" design, a criticism which can be approached if the side-effects are systematically recorded at each assessment point and then submitted to statistical comparison between groups.

MICHAEL ROBINSON
GIRISH SHETTY

Department of Psychiatry
University of Liverpool

Unilateral Auditory Occlusions and Auditory Hallucinations

SIR: After McGuffin noted that schizophrenic patients with auditory hallucinations sometimes plug their ears (*Journal*, June 1979, **134**, 651–652), Green suggested that plugging just one ear may help (*Journal*, September 1979, **135**, 287). Finding impaired binaural vs monaural verbal comprehension in schizophrenics, Green & Kotenko (1980) reasoned that plugging the inferior ear (usually the left) would improve comprehension and might ameliorate auditory hallucinations. Concurrent with another intervention, James (*Journal*, November 1983, **143**, 515–516) tried unilateral ear plugging (UEP) for auditory hallucinations. He concluded that the associated improvement was not due to UEP because plugging either ear helped. While inconsistent with the hypothesis that only UEP of the inferior ear should help, other notions about UEP could accomodate these findings. The need for other hypotheses about the UEP effect is further raised by a case we wish to report. For this patient with chronic hallucinations, plugging the superior comprehending right ear was followed by a striking decrease in auditory hallucinations. The effect outlasted the period of occlusion, and even persisted into an exacerbation of psychosis.

UEP had no effect on four other actively psychotic chronic schizophrenic men, but perhaps their heterogeneity was a factor. Compared with the others, the patient who benefitted was younger, better adjusted premorbidly, and was more reactive to life events. He had more florid positive and less marked negative symptoms, and was relatively more neuroleptic-responsive.

Case report: This right-handed 32-year old with chronic paranoid schizophrenia (DSM–III) had experienced frequent exacerbations, and was in hospital when UEP trials began. While other symptoms were neuroleptic-responsive, medication did little for his loud, nearly continuous hallucinatory 'voices'. He had heard them daily for six years. He was symptomatically stable for several months, and no change was made in medication or dose (chlorpromazine 400 mg, p.o., TID) for a month before, and during UEP trials. An independent rater assessed auditory hallucinations at base-line as severe (BPRS score = 6).

The patient had normal hearing on audiometric testing. On Green & Kotenko's (1980) test, his right ear comprehension score (27/40) was better than both binaural (22/40) and left ear (13/40) scores. Plugging the inferior-comprehending left ear ten hours daily for five days did not yield the predicted therapeutic response.

Three days after left UEP was ended, right UEP was begun. After two days, the intensity, clarity, and frequency of his auditory hallucinations markedly decreased (BPRS ratings = 2 (very mild) or 3 (mild)). Anxiety, excitement, suspiciousness, and unusual thoughts also diminished. Comprehension increased on all tested conditions, especially in the left ear. Three weeks of right UEP was associated with continued improvement. During this time he was well enough to be discharged, and he went without UEP for two months, with only rare, soft, and indistinct hallucinatory 'mumbling'. Visual, but not auditory hallucinations gradually developed. A few weeks after readmission, right and left plugs were sequentially tried, but without effect. Auditory hallucinations did not recur until several months into this relapse as his general condition worsened. As the primary investigator had left the city, UEP was not again tried.

While not proving the efficacy of UEP this case strongly suggests it, and the recurrence of psychosis without auditory, but with visual hallucinations implies that UEP effects were modality-specific. Cross-modal 'compensatory' processes may have led to the emergence of visual hallucinations. This result with UEP opposite to the predicted side requires an alternative formulation to Green & Kotenko's (1980) model. One possibility is suggested by the reduced right hemisphere evoked response to left ear stimulation in schizophrenia (Connolly *et al*, 1985). By limiting auditory input to the left ear, a right ear plug might enforce better engagement of right hemisphere attention. There is also evidence of left hemisphere overactivation and dysfunction in schizophrenia (Gruzelier, 1983). By nearly eliminating right ear input, right UEP may help to normalize left hemisphere activation and function. The relevance of this to auditory hallucinations is suggested by the fact that plugging the ear contralateral to the affected hemisphere alleviates auditory illusions associated with temporal lobe epilepsy (Jacobs *et al*, 1973). UEP could interfere in several ways with processes underlying auditory hallucinations.

STEPHEN E. LEVICK
ERIC PESELOW

Yale University
V.A. Medical Center 116A/1
West Haven, CT. 06516, USA

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Awake, Perchance Asleep?

SIR: It is generally agreed that patients suffering from depression show reduced Sleep Efficiency, decreased Slow Wave Sleep and latency to REM, and changes in the distribution of REM sleep. Some recent models of depressive illness have been based in major respects on these findings (Borbely & Wirz-Justice, 1982; Wehr & Wirz-Justice, 1981). However, recording of the EEG has been restricted to the nocturnal sleep period in the studies demonstrating these abnormalities of sleep. Studies in normal subjects show that the duration of preceding wakefulness has a profound influence on subsequent sleep (Borbely, 1982), and that daytime naps may result in nocturnal sleep which has two of the main features shown in depressed patients: decreased Slow Wave Sleep and REM Latency (Karacan *et al*, 1970). We are aware of only one study in which the EEG of depressed patients was recorded over a 24 hour period: the average duration of daytime sleep was 5.7 hours (Shimizu *et al*, 1979). Because patients in this study were selected on the basis of complaints of increased sleepiness and time in bed, the results may be biased, though to what extent cannot be determined.

Precise information about the occurrence of sleep over 24 hour periods in a random sample of patients would be required to define more specifically the EEG characteristics of sleep in depression. Some information can be obtained by behavioural observation. On the Treatment Evaluation Unit at the Kingston Psychiatric Hospital we obtained behavioural observations in 20 randomly selected patients suffering from major affective disorder (depression) according to DSM–III criteria (three bipolar, 17 unipolar; mean age 53.3 years). Over periods of at least five days of observation for each patient, all showed episodes of bed rest when seen at half-hourly intervals between 0800 and 2100 hrs. Bed rest was noted on 62% of the observation days, with a mean duration of 2.6 hours. Although in this sample we cannot rule out the possible sedating effects of psychotropic medication, this finding supports the notion that daytime sleep may occur frequently in depressed patients not selected for increased daytime sleepiness.

Behavioural observation may, however, underestimate the amount of sleep that occurs. We have now obtained a continuous EEG record of sleep activity over the last eight hours of a 48-hour sleep deprivation in a depressed patient. The record was made with a portable cassette monitoring system (Oxford Medilog). During the time of presumed wakefulness the patient accumulated 11.1 minutes of Stage 2 sleep. In most instances the episodes did not exceed 20 seconds in duration; the shortest was as brief as four seconds and the longest was 48 seconds. In addition, longer episodes in the record showed slowing of the EEG, in the absence of eye movements, which were not scored as sleep because the wave forms did not meet the formal amplitude criterion. There were also many instances of sleep spindles against a background of eye movements and alpha frequency EEG. In spite of the patient's excellent co-operation in trying to keep awake, and constant observation by the nurses, neither they nor the patient were aware of the occurrence of sleep, though the latter had felt drowsy at times.

These observations indicate the need of continuous recording of EEG to verify presumed wakefulness in studies on the effect of sleep deprivation in depression. They also call into question previous attempts to explain the origin of the sleep disturbance typical of these patients, raising the possibility that it may be, at least in part, a consequence of the daytime discharge of non-REM sleep.

S. E. Southmayd
J. Cairns
N. J. Delva
F. J. J. Letemendia

Kingston Psychiatric Hospital
Kingston, Ontario K7L 4X3
Canada

D. G. Brunet

Kingston General Hospital
Kingston, Ontario K7L 2V7
Canada

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Capgras Syndrome

Sir: I wish to report two cases of Capgras syndrome for time, a previously unreported phenomenon. Each patient also suffered from multiple other misidentification syndromes.

Case reports: (i) Ms A, a 33 year old white female with paranoid schizophrenia (DSM–III), had chronic delusions that multiple persons had been replaced by physically identical imposters who were either anonymous persecutors (Capgras syndrome), or specific other people (Fregoli syndrome). She also believed that certain places were identical duplicates of other locations known to her (reduplicative paramnesia). In addition she reduplicatively misidentified time, believing that 1984 was 1991. This occurred either episodically or simultaneously. At different interviews she might assert that it was 1984, or 1991, or both. It is important to note that she truly believed that two different periods of chronological time existed simultaneously—as opposed to being disoriented for an misnaming the true time in which she lived.

Her history and physical examination were negative for neurological abnormalities. Computerised tomography (CT) of the head, positron emission tomography of the brain, and evoked potentials were normal. Electroencephalography showed slow wave activity with lateralised predominance to each hemisphere at different times. Neuropsychological testing showed bilateral parietal and frontal lobe dysfunction on a pattern of diffuse right hemisphere dysfunction.

(ii) Mr B, a 31 year old white male with paranoid schizophrenia (DSM–III), had chronic delusions that duplicates of himself existed (syndrome of subjective doubles), that certain individuals were not only duplicates of others, but also looked like them (syndrome of intermetamorphosis), and that certain individuals were specific other people (Fregoli syndrome). He also had the longstanding belief that time was duplicated and that he existed in both the present and another time in which he was aged 82. When he thought he was in the future he believed that the entire world was also in the future, although he did not misidentify his surroundings. As with case (i) he had the delusion that two periods of chronological time simultaneously coexisted.

His past history was notable for three head injuries with loss of consciousness, one with coma requiring ventilation. His family history was positive for mental retardation and alcohol abuse. Physical examination and routine laboratory evaluation were unremarkable. EEG was within normal limits, and CT scan revealed bilateral frontal, temporal, and parietal lobe atrophy.

Classical misidentification syndromes include Capgras syndrome, Fregoli syndrome, syndrome of subjective doubles, syndrome of intermetamorphosis, and reduplicative paramnesia (Christodoulou, 1978; Joseph, 1986). It has also been suggested that psychotic syndromes of disorientation for place or time and reduplication of body parts are misidentification syndromes (Weinstein *et al*, 1954). The essential feature of these is a chronic psychotic misidentification of person, place, time, or other object, usually (but not always) with psychotic reduplication of that object. Weinstein *et al* (1954) discussed reduplication for time, but the case reports suggested psychotic disorientation for time rather than the belief that more than one time existed simultaneously. The cases reported here extend the range of psychotic reduplicative misidentifications to include not only person, place, and object, but also time.

ANTHONY B. JOSEPH

McLean Hospital and
Massachusetts Mental
Health Center
Boston

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SIR: The Capgras syndrome is the rare delusional belief that person(s) important to the patient have been replaced by identical doubles. Included in this is the belief in a double of the patient himself or herself masquerading as the patient but never actually perceived. Of the 133 cases of the Capgras syndrome reported in the English language literature since 1923 and reviewed by Berson (1983), eight cases showed this latter form of the syndrome and of these only three patients in the 50 years believed that they themselves were the double.

Case report: The patient, RS, was reviewed recently when the doctor involved was asked to cover another doctor's duties in a different hospital. RS and the doctor had not met for 10 years, and the patient gave no sign of recognition. After a few minutes, RS stated that this wasn't the RS that had been known previously. That RS had been replaced by a baby of 8 months, or perhaps 2 years, made in a big machine in the main hospital building and ironed out to the patient's size and made to look like the patient.

When seen a few days later the patient persisted in the same delusion but admitted remembering the doctor. How was this? The other RS had passed the information on. In the past, three or four people had masqueraded as RS. Two had since died, one may have been murdered and one married. RS said her father was coming to visit her, and that she sometimes felt an injection in her ear which meant she had to say "aaah" out loud. RS was well oriented and denied feeling depressed, although the nursing staff reported her to be weeping and sad at times. Her chief amusement was smoking. Did she like reading books? No, she couldn't read, being so young.

RS came of a large family and both parents were dead. She qualified professionally in England and had three psychiatric admissions before being admitted to this hospital in 1966 at the age of 25.

From the case notes, in which she was given a diagnosis of schizophrenia, her mental state had changed little over the years. Various paranoid, hypochondriacal and grandiose delusions predominated. She was also noted at times to show incongruity of affect, thought disorder, lack of concentration and insight, poor motivation, ideas of reference and occasional episodes of aggression. There were no reports of depression, disorientation, flight of ideas or overactivity of any sort. Occasional non-verbal hallucinations had been reported.

In 1980 RS had bilateral mastectomies and chemotherapy for lobular carcinoma of the breasts. In 1982, according to her case notes, she claimed not to be RS but a two year old male called Jonathan. She was surrounded by a large invisible plastic box. Another note, in 1983, showed that RS claimed to be a three month old baby in her father's womb. In 1985 a chest X-ray showed metastases in the ribs and sternum.

Current medication included analgesics, anti-emetics, haloperidol, trifluoperazine, fluspirilene and biperiden. The patient was up and about and rarely requested analgesia.

Although organic factors could be postulated, it is easy to understand the denial, the wishful and fearful concrete regressed thinking that has wrought a delusion of being her own facsimile in this woman now so sadly placed on the edge of life.

A. SCHOFIELD

Regional Hospital
Wilton, Cork
Republic of Ireland

Reference

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SIR: In contrast to the oldest patient with the Capgras syndrome (*Journal*, December 1985, **147**, 719–729), I would like to report a case of a 14 year-old adolescent female presenting with a 'delusion of doubles'.

Case report: The patient was admitted to an in-patient child psychiatry unit with a 12 month history of increasing irritability, weepiness and deteriorating school performance, becoming more evident six months prior to admission. Mental state examination revealed a delusional belief that her parents were imposters and that her real parents had had her adopted at the age of six. She identified her real father as being a well-known English rock musician. She maintained that the pictures of herself as an infant were those of her double with whom she had been swapped at the age of six and who was currently living in England in her place. She also manifested clear ideas of reference when listening to the musician's records. She recalled 12 months previously experiencing a sudden realisation as to who her real father was when listening to one of the musician's records. This autochthonous delusion persisted from that time. At admission she appeared perplexed, agitated and mildly thought-disordered. Family history revealed that the child's parents separated when she was an infant. Her biological mother had remarried when the child was nine. There were two other female step-sisters in the family, both of whom were well. There was a positive family history of paranoid schizophrenia in the mother's 30 year-old younger sister, beginning when she was aged 16 years. Physical investigation of the patient, including a CT scan and EEG, were unremarkable.

The patient improved symptomatically during the course of hospitalisation. She was treated with neuroleptics. However, her idea of doubles persisted with reduced intensity. She revealed to her therapist that she had experienced an incestuous relationship with the maternal grandfather when she was approximately six years old. In addition, she claimed to have been "raped" by a boyfriend six months prior to admission. Psychosocial investigation substantiated the earlier claims of incestuous experience at the hands of her grandfather.

This is the youngest reported case of a Capgras syndrome emerging within the context of a paranoid psychosis (Berson, 1983; Enoch, 1980). Whilst there was no evidence of organic brain pathology, there was clear evidence of a shy, sensitive personality development in the patient and a positive family history of paranoid schizophrenia. The interplay of the predisposing incestuous experience combined with a further sexual insult appeared important in the development of the acute psychotic reaction described.

LAURENCE JEROME

Madame Vanier Children's Services
871 Trafalgar Street
London, Ontario
Canada N5Z 1E6

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Oral Habits – A Behavioural Approach

SIR: Oral habits are very common in childhood and include nail-biting and finger-sucking, teeth-grinding, mouth-breathing and lip-chewing. They are often associated with psychological problems. I would like to outline the treatment of a 12 year-old boy presenting with nocturnal lip-biting, which resulted in tissue damage and ultimately repair by plastic surgery.

Case report: S was referred by a paediatrician. He had an unsightly, swollen and protuberant lower lip which appeared to be the result of lip-biting during sleep. His mother had noticed blood and saliva on her son's pillow for about two years, but the lip had been obviously swollen following a bout of mumps eighteen months ago. There was no evidence of lip-biting during the day. No precipitating cause was evident for the behaviour, and the boy showed good adjustment both at home and at school.

Star-charts have been used extensively in child psychiatric practice as a way of re-inforcing desired behaviour. After the first interview, S was started on a star-chart which was explained to him in detail. He and his mother were to check his pillow each morning for blood and saliva, i.e. evidence of lip-biting. If present, the chart would remain blank for that day, but a clean pillow would result in a blue star. Three blue stars in a row would merit an extra gold star and some kind of reward to be negotiated between S and his parents. He was advised not to get too down-hearted if he did bite his lip one night but to try again the next night.

The family were reviewed after three weeks, and at this stage S had achieved a star nearly every night. Over the next six months S was reviewed at intervals and the lip-biting soon stopped completely. During this period, S was referred to a plastic surgeon as the lip remained unsightly despite the oedema having settled. The lip is to be surgically repaired within the next few months.

A search of the literature reveals relatively few papers on lip-biting, and these tend to be found in the dental journals. Turley & Henson (1983) conclude that lip-biting is associated with a number of organic and functional disorders. The management depends on the medical history of the child, the aetiology of the behaviour and the severity, frequency and method of inflicting injury. Mentally retarded and autistic children often exhibit severe lip-biting which may be associated with an altered pain threshold. The Lesch-Nyhan syndrome is a specific sex-linked disorder characterised by hyperuricaemia, choreoathetosis, mental retardation and self-mutilation. LaBanc & Epker (1981) describe a case where repeated lip-chewing resulted in destruction of the lower lip and the need for surgical intervention. Normal as well as mentally retarded children often bite the lower lip following an initial dental visit where a local anaesthetic is used. Gilmour *et al* (1984) describe lip-biting in a sixteen year-old girl under the influence of interior dental nerve-block analgesia, complicated by solvent abuse, and resulting in tissue loss. Trauma to the lip is well-known to occur as a result of epilepsy.

Lyon (1983) describes the treatment of lip-biting in a 12 year-old boy of normal intelligence using behavioural techniques (tracking, aversive response substitution and relaxation training). Other treatments seem to concentrate on the use of intra-oral appliances.

I found no mention in the literature of lip-biting during sleep, but it appears that the use of a star-chart in this circumstance may lead to a prompt and effective response.

M. P. J. Ellis

Department of Child Psychiatry
St James's University Hospital
Leeds

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Lithium-Induced Reaction

Sir: I wish to report a patient who has recently suffered a rare combination of side-effects with lithium carbonate—hair loss and severe acneiform lesions during a three month course of this drug. Although both of these side-effects have been reported very infrequently the combined effects in such a short space of time have not been documented.

Lithium is an alkali metal which is known to accumulate in hair (Kusumi, 1971), and hair loss of varying degrees can occur in the absence of pathology with normal lithium levels (Mortimer, 1984; Muniz, 1982). Often the hair loss subsides despite continuation of the drug. Other cases have reached alopecia totalis, the drug being then discontinued; in all cases the hair re-grew back to normal. The same response can be observed with regard to acneiform eruptions, which can occur in varying degrees, all skin reactions clearing up either with drug continuation or cessation (Okrasinski, 1977; Vacflor, 1970). The above phenomena occur predominantly in females.

Case report: The patient was a 47 year old woman who had suffered from chronic manic-depressive illness for over twenty years. Her physical health was good, although she had undergone a hysterectomy for severe endometriosis five years previously. She also suffered from mild acne in her teenage years. She had never taken lithium prior to this course.

In early November 1985 she was started on lithium carbonate (250 mg t.d.s.). Physical examination, including thyroid and renal function tests, were normal. Within two weeks lithium was increased to 250 mg q.i.d., and kept at this dose as her serum lithium levels were within acceptable limits (0.7–0.9 mEq/L). Her mental state improved considerably over the next month—so much so that she was discharged from hospital following a nine-month admission. On the sixth week after commencement, she complained of sudden generalised hair loss. This was quite severe, but eased by the ninth week. Serum lithium levels remained within normal limits during this time. As the hair loss subsided, the patient noticed small acneiform eruptions over her neck and face. These became painful, enlarged and pusy, and this continued in varying degrees of severity until the thirteenth week—at which time the drug was discontinued. Within two weeks her skin condition had almost completely recovered, but unfortunately her depression had returned and readmission was necessary.

It should be pointed out that over this time the patient opted to remain on lithium despite the hair loss and skin eruptions as her mood disorder had improved considerably. I would be grateful for further comment by any colleagues who may have encountered similar reactions with this drug.

Denis P. Eustace

Hampstead Private Hospital
Glasnevin
Dublin 9

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Psychiatric Manifestation as an Early Symptom of Behçet's Disease

Sir: Neurological involvement is seen in approximately 25% of patients with Behçet's disease (BD). In general, these complications develop in the late stage of the disease when major physical symptoms such as recurrent oral ulcers, uveitis and skin eruptions have already occurred. Psychiatric symptoms usually occur as incidental findings in about half of the patients with neurological involvement (Pallis & Fudge, 1956; Shimizu, 1972).

The patient described here developed prominent psychiatric symptoms without neurological abnormalities in an early stage of BD when the diagnosis had not been established. Such a case has not been described in the literature.

Case report: The patient, a 44 year-old Japanese female, was admitted because of sudden onset of general malaise, emotional lability and tactile hallucination ("a thick piece of leather is stuck on my body"). On admission, her responsiveness was good. Physical examination showed no abnormal findings except for oral ulcers. Elevation of ESR and mild leucocytosis were found. She had a two-year history of recurrent oral ulcers and a recent genital ulcer, and had been suffering from family trouble for a few months. It seemed that the family trouble played a part in the psychiatric symptoms. Within a few days of admission, however, delirium with visual hallucination and stereotyped behaviour (e.g. praying, echolalia and increased psychomotor activity) developed, and she was transferred to a psychiatric ward. No neurological signs were found. CSF findings revealed slight lymphocytic pleocytosis (71/mm^3). EEG showed irregular poor alpha activity with mild diffuse slowing. A computerised tomography scan was normal. Although skin puncture test was negative, we suspected BD with CNS involvement, and treated her with prednisolone for about ten weeks (starting with 60 mg/day and decreasing gradually). The drug had a marked beneficial effect on the psychiatric symptoms, and laboratory abnormalities and CSF findings returned to normal. However, she gradually became indifferent to her surroundings and unable to learn new information. Five months after initial hospitalisation she was discharged.

Six months later, she developed skin lesions (furuncle-like pyoderma) on her back. At this time, the diagnosis of BD was confirmed according to the diagnostic criteria of BD in Japan (Behçet's Disease Research Committee of Japan, 1982). Seven months later, she showed mild hemiparesis in the right limbs.

Psychiatric episodes in an early stage of BD may be misdiagnosed and mistreated as psychiatric illnesses such as schizophrenic disorders (Shindo, 1973). When a patient with only a few physical symptoms characteristic of BD develops a mental disorder, the psychiatrist should be aware of the possibility of the disease. Careful evaluation of the patient's history and biological data may give a clue to the diagnosis.

SHIGERU CHIBA
SABURO TAKAHASHI
TSUTOMU MIYAGISHI

Asahikawa Medical College
Asahikawa, Hokkaido, 078
Japan

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Small Correction

SIR: I read with interest the case of 49XXXYY Chromosome Anomaly (*Journal,* February 1986, **148,** 210–212). His height of 1.7 cm suggests serious competition for Tom Thumb as the world's smallest man. We have all heard of the Cardiff giant, and now this.

ERIC W. FINE

Alcohol and Mental Health Association, Inc.
1200 Walnut Street, Second Floor
Philadelphia, Pennsylvania 19107

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Book Reviews

The Real Self: A Developmental, Self, and Object Relations Approach. Edited by James F. Masterson. New York: Brunner/Mazel. 1985. Pp. 183. $25.00.

Masterson is an American psychiatrist with special experience of psychotherapy with borderline psychotic and narcissistic personality disorders, the "disorders of the self" in the current analytic parlance of America. Psychoanalytic theory there was dominated throughout the 1970s by "the psychology of the self". This was noisily controversial on every issue, from diagnostic definition to expectable transference patterns and the timing of interventions. The clinical evidence from the two main contending camps tended to come from lengthy, strictly controlled psychoanalyses; the cautious sophistication of the theoretical conceptualisations understandably left many general psychiatrists irritable and impatient. What good, they asked, was all this erudition, if it did not provide for them unambiguous and trustworthy guidelines for the management and therapy of the many such cases under their care. Such usefulness does filter through from experimental psychoanalysis to general psychiatry, but it is inevitably partial, and often slow, as it has been in this case.

Masterson seems well placed professionally to mediate such filtration, and I was hopeful of the book in this respect. However, I was left disappointed. His scheme for understanding and intervening, elaborated well in Section 1, clearly works *for him*. It is a personal solution; but it seemed to me, especially when I read the non-clinical Sections 2 and 3, that his technique is very tailored to his own personality, and lacks general applicability.

The general background of his approach is conventional enough. Confrontation of the narcissistic character defences evokes a specific mix of anxiety and depression, "abandonment depression", which is characterised by a frightening sense of helplessness. This is contained and worked through, until the resulting new stabilisation allows the next confrontational loosening of character defences, etc. The nub of Masterson's own personal technique, "communicative matching", is that at the point where the patient's sense of helplessness is most searing, he intervenes authoritatively with an active, educative line.

A selected active project, such as a work of art or a legal venture, is recommended, and Masterson educates the patient vigorously regarding this practical aspect of his or her life. The author warns us emphatically that such interventions may be improperly timed, with counterproductive results, and that this premature intervention is brought on by the near intolerable boredom and despair the therapist must endure in the countertransference in the phase of abandonment depression. Of course the skeptical reader puzzles, and wonders if these two courses—the recommended right one and the proscribed wrong one—might not be one and the same; or to put it another way, who but Masterson could know—for Masterson—which was which?

Then the non-clinical Sections 2 and 3 come as a shock, one that could lead to a too hasty undervaluation of Section 1. The brashness and shallowness with which the author stomps around outside his field, diagnosing self-disorders in everyone from Snow White and Jean-Paul Sartre to the entire civilisation of Japan, leaves no doubt that here is someone who, on one side of his personality at least, would be capable of inadvisably telling people how to run their lives. Still, to retrospectively pass a negative judgement on the clinician of Section 1 could, paradoxically, be quite mistaken.

Speaking of "selves", the central instrument of any psychotherapist is his or her self, and many produce their best and/or worst contribution in the area where their own personality is most needfully prone to conflict. On the pragmatic value of Section 1, therefore, I return an open verdict. The individual reader will have to decide for himself. I will say this: after encountering Sections 2 and 3, it makes a far more interesting read!

DENNIS DUNCAN, *Psychoanalyst, London*

Psychiatry: The State of the Art. No. 5. Child and Adolescent Psychiatry, Mental Retardation and Geriatric Psychiatry. Edited by P. Pichot, B. Berner, R. Wolf and K. Thau. New York: Plenum. 1985. Pp. 504. $55.00.

While the reviewer of this volume, covering so diverse a range of topics, should ideally have omniscience, he can only reflect that after all, most psychiatrists are generalists.

This volume is the fifth in a series edited by Pichot, Berner, Wolf and Thau of the papers presented at the VII World Congress of Psychiatry in

Vienna, 1983. The editors of the proceedings had the daunting task of dealing with a very large number of presentations. They solved the problem by restricting publication to proceedings of plenary sessions and symposia. They also had to strike a balance between collecting together cognate subjects which might produce a large number of very small volumes or to compromise and group them together in such a way as to allow people to purchase only certain sections in which they were interested. Hence this volume has a wide range of topics varying considerably in relevance and quality. Nevertheless there emerges a theme of cross-cultural comparisons in psychiatric research and services which is invaluable to those interested in obtaining an overview of world psychiatry.

The section on child psychiatry contains chapters on classification and nomenclature, risk and vulnerability (E. J. Anthony), anorexia nervosa (W. Rickards), and US teaching of child psychiatry (R. R. Rogers). There are also many chapters on organic topics and manic-depressive illness. The section on treatment in child psychiatry emerges as rather idiosyncratic in its coverage of the topic: there are two chapters on lithium, one on altered prolactin response in anorexia, and another on artistic media in therapy.

The section on social and transcultural child psychiatry is of particular interest, with chapters concerning screening of children in Japan, the use of the Rutter scale with Indo-Chinese children, minor psychiatric illness in mothers of young children, etc.

There is an extensive coverage of puerperal mental illness with papers by Cox (on sociocultural determinants of postnatal depression), Brockington (on definition), Kumar (on aetiology and consequences) and Wrate *et al* (on subsequent child development).

Perhaps the most useful section of the volume is that on mental retardation, which is very extensively covered. There are chapters on psychiatric syndromes affecting the institutionally mentally retarded (Mulcahy), schizophrenia in the retarded (Menolascino) and epidemiology (Pilkington). There are also chapters on treatment and community-based programmes with particularly good coverage of day treatment.

By far the biggest section is that on geriatric psychiatry, to which approximately half of the volume is devoted. There are sections on the dementias in late life, the psychophysiological disorders of old age, neurotransmitters in the dementias and dementias as multi-stage processes. There is an excellent coverage of mental deterioration in the aged emphasising diagnosis and management.

Tom Arie's paper on psychogeriatrics and the family doctor emphasises areas of collaboration at primary levels of care. In the section on services to the elderly the emphasis is placed on programme evaluation. Barry Gurland deals with the paradoxical relationships between services, needs and outcome, and Jolley and Wilkin cover the problems of patients and relatives at referral. A particularly interesting paper is that by Ten Horn on the boundary between psychiatry and gerontopsychiatry, using data from the Groningen Psychiatric Cases Register to illustrate graphically the importance of epidemiological monitoring of services. She substantiates the case for psychogeriatric services confining themselves to people aged 75 years and over since the younger elderly are so similar to other adults in middle life. There are several chapters on day hospital care for the elderly. Anyone concerned with planning of psychogeriatric services would do well to consult this volume since a wide range of countries and approaches is covered.

This volume was prepared from "camera ready scripts" provided by the authors at the time of the Congress. The result is less than pleasing aesthetically but in most cases provides a serviceable script. However, those authors with better typewriters are easier to read! Another criticism would be that since the index is built up from keywords also provided by the authors, it tends to be rather skimpy for a volume of this size.

The book has a list price of $55.00 which may restrict sales to medical libraries or the shelves of proud contributors. It is nevertheless a useful reference book.

R. J. DALY, *Professor of Psychiatry, Cork Regional Hospital, Cork*

Mental Disorders, Alcohol and Drug-Related Problems, International Perspectives on their Diagnosis and Classification. A Joint Publication by the World Health Organization and the Alcohol, Drug Abuse and Mental Health Administration. International Congress Series No. 669. Amsterdam: Elsevier. 1985. Pp. 600. US $111.00/Dfl. 300.00.

In 1982 a major conference on the *Classification and Diagnosis of Mental Disorders* was held in Copenhagen, under the auspices of the WHO and ADAMAR (Alcohol, Drug Abuse and Mental Health Administration of the USA). It was perhaps the most comprehensive conference of its kind, both in the breadth of its representation, involving forty-seven countries, and in the fact that the whole of psychiatry was reviewed.

Important reasons for the conference included concern that at a time when there was considerable activity in many countries in mental health programmes, there were trends inimical to the agreement of a diagnostic system and classification.

This volume is in essence a Conference Proceedings, complete with reports of plenary sessions, discussions and workshops. The latter include recommendations.

Sections include the current studies on diagnosis and classification; strategies and methodologies used; the contribution that psychopathology can make to classification (remembering as Professor Ebie from Nigeria points out ... "Whilst psychological phenomena are universal experiences, what is different from race to race and country to country is the language with which patients relate their experiences"); the implications of clinical and treatment outcome, research on classification, the contributions being made by biological research (at present looking exciting, but clearly at an early stage); the role of epidemiological research, an examination of cross cultural aspects of classification; problems of the classification in the field of personality patterns and disorders; and the contribution that psychosocial and behavioural sciences can make to diagnosis.

It is not an easy read. The language is technical and requires a high academic standard of knowledge, not only of psychiatry but of classificatory systems, logic and other disciplines. It is the functional psychoses which predominate and it is clear that whilst in many countries the fundamental diagnostic differentiation into schizophrenic affective disorders and other psychoses is widely used, beyond that there is little agreement.

Further, there are clearly classifications, such as in France and Scandinavia, which appear idiosyncratic and which have not obtained general support. It is also evident that in the schizophrenic group of disorders there remain considerable problems regarding reliability of diagnosis and whether schizophrenia can be continued to be regarded as a single entity. Contributors to the conference expressed a very wide range of opinions in relation to the future successes in establishing an agreed classification of mental disorders, varying from gloom to optimism.

What does this book offer to the ordinary psychiatrist on the top of the "Clapham Omnibus"? I do not think a great deal, except perhaps to make him aware of how little we really know about diagnostic entities in psychiatry and to shake complacency about our present knowledge. This book, however, is not intended primarily for this audience, but as a reference text for academics and psychiatrists working in this field. For them it is a major work and likely to be an academic milestone.

BRIAN D. HORE, *Consultant Psychiatrist, Withington Hospital, Manchester*

Mental Heath Services in Europe: Ten Years On. By H. L. Freeman, T. Fryers and J. H. Henderson. Copenhagen: WHO Regional Office for Europe. 1985. Pp 112. Sw.Fr. 11.00.

The authors have made a brief assessment of the impact made in Europe by the long-term mental health programme promoted by WHO. The period covered is 1970–1982, during which major changes occurred, notably in the UK and Italy. The WHO programme has consisted mainly of seminars and workshops leading to the promulgation of memoranda of guidance that have doubtless played some part in bringing about the now general consensus in favour of a broad range of "community" psychiatric services rather than concentrating the provision of care in large hospitals.

The limited nature of their remit means that the authors are unable to say very much more than this. They point out the well-known deficiencies in national data collection, thoroughly summarise the information that is available and cautiously conclude that there has been a general improvement of the kind WHO would like to see. It was a job worth doing and provides a useful alternative to the usual bearing of witness to great works.

The general tone of the document is neutral to the point of being bland, but the narrative does contain an occasional flash of criticism. For example, "Italy's adventurous Mental Health Act of 1978 has raised major problems of implementation, and it is possible that the country could learn from the experience of France in preparing for major changes in services in such a way as to allow their progressive implementation". And, on primary prevention: "[It] remains such an attractive goal—with the prospect even of financial savings in the long run—that demands continue to be made for services to be reoriented in this direction, even if it is not clear what they are then expected to do". The authors criticise "diffuse, vague and over-ambitious" proposals made in WHO documents and grand statements to the effect that communities "must be mobilised" and "accept their responsibilities" in order to bring about community care.

Some real advances in the provision of medical information systems that will allow comparison between services in different countries will come from efforts being made to adopt similar standards for basic data collection in psychiatric case registers, of which there are now a dozen or more throughout Europe. Registers have the potential to provide information about the problems and therefore the needs of individuals, which, collectively, can serve as the basis for "bottom-up" planning. WHO is well placed to foster the network and to persuade national governments to recognise their value.

JOHN WING, *Professor, MRC Social Psychiatry Unit, Institute of Psychiatry, London*

Normal Aging, Alzheimer's Disease and Senile Dementia—Aspects on Etiology, Pathogenesis, Diagnosis and Treatment. Edited by C. G. Gottfries. Belgium: Edition de L'Université de Bruxelles. 1985. Pp. 312. 992 FB (Belgian francs).

Last year two symposia were held at the Collegium Internationale Neuro-Psychopharmacologicum 14th Congress in Florence and the various speakers were invited to prepare written contributions covering their presentations. This book constitutes a compilation of those papers. The first half is divided into two sections: aetiological and pathological aspects.

Unfortunately, these category distinctions are not clarified by the overlapping variety of papers in each section. The chapters, although rich in material, do not form a cohesive whole and behavioural, animal model and epidemiological studies occur in a sequence without apparent logical connection. No attempt is made by the editor to summarise salient points from some very discursive accounts and the contributors do not always draw conclusions from their own work. Most of the papers are no more than 6 pages in length and range from unreferenced to a list as long as the paper itself! Recent advances in investigative techniques in the neurosciences are illustrated by receptor binding studies using radio immuno-assay methods and these form the basis of the best papers in these sections. Of particular interest is the paper by a group of Finnish workers on dementia and brain receptor changes in Parkinson's disease.

The second half consists of diagnostic and treatment sections; diagnostic aspects largely concentrate on the valuable new radiological imaging techniques of positron emission tomography and proton nuclear magnetic resonance imaging. These contributions from renowned USA centres are worth attention, as indeed is a useful chapter on clinical profiles and Alzheimer's disease which will appeal to the general psychiatrist or psychogeriatrician.

The treatment section is disappointing in giving limited guidance about hopeful approaches for the future. Various contributors argue similarly that it is too optimistic to believe that any one drug can compensate for a wide range of disabilities in so far as dementia is a generalised cerebral disease. Neurotransmitter precursors, enhancers, neuropeptides and vaso dilators have been demonstrated to be largely ineffective in clinical trials and this conclusion is made in the last three chapters.

It is no easy task to do justice to such a complex subject and the book does, in fact, succeed in drawing together current knowledge from a variety of fields of interest. This achievement must recommend it for an appropriate place in the libraries of research and teaching departments of psychiatry.

M. R. LOWE, *General Psychiatrist, Basildon Hospital, Basildon, Essex*

Emerging Issues in Child Psychiatry and the Law. Edited by Diane H. Schetkey and Elissa P. Benedek. New York: Brunner/Mazel. 1985. Pp. 378. $37.50.

This is an American multi-author text and is a welcome sequel to the editors' earlier work *Child Psychiatry and the Law*. It will appeal to all who practise in the field of child and adolescent care. The authors appear well chosen for their competence and experience, and the editors have ensured good coverage of the topics chosen. Perhaps there would have been a place for a chapter by a practising lawyer, or by a professor of jurisprudence; as it is, the preponderance of the material comes from the psychiatric authors, although social work and psychology are represented.

British readers may find that some of the details and the issues discussed are not directly applicable to their work. This is because the American approach to the subject of child care tends to be more legalistic than obtains in Britain, because the cases cited based upon the system of State and Federal appellate systems, and the influence of the Supreme Court, are unfamiliar, and because some of the more contentious issues under active American academic and legal discussion and review are at a less advanced stage of collective deliberation in Britain, although the possibility of a Family Court is already envisaged here. This is not to detract from the general interest of the book to British readers, since our child care and legal systems will in time have to reach considered solutions to much of what it discusses, and several of the more practical chapters have direct clinical relevance now.

An abridged description of chapter subjects will indicate the scope of the text. There is a main section on ethics, in which are treated ethics in child psychiatry, the capacity of children to participate in decisions affecting them, under what circumstances treatment is refused for child cancer patients, and a final chapter on organ transplants and research. The next section deals with child custody, with chapters about the provision of reports, the role of mediation, joint custody, custody by the father, the importance of male and female homosexuality to custody and access decisions, the role of grandparents, and how allegations of sexual abuse should be evaluated.

The third main section is about the juvenile offender. It starts with a detailed review of the juvenile court system with its changing aims and concepts. Then there is a chapter about when juveniles may be tried in adult courts, and lastly a review of treatment alternatives. There are two final sections on special issues and emerging issues. In the former is a discussion of the beneficial effects of the 1975 US legislation about the education of handicapped children, psychiatric admissions of children and adolescents, psychiatric approaches to cults, role models for violence and examinations of children subjected to violence. The three final chapters on emerging issues concern the ways in which young babies can assist in court hearings, the experience of a psychoanalyst in developing new ways to work with children, and a review chapter of what the authors judge to be emerging issues in the 1980s.

At the price quoted it may be expensive for individuals but anyone working in this general field would find it of interest, a useful source of references and a thoughtful presentation of complicated matters with which any developed society must sooner or later grapple. The book is a balance between practical chapters and academic discussions of a stimulating kind. I hope that libraries in the relevant disciplines will find a place for it, and that extracts from it will form the subject of many teaching seminars.

OLIVER BRISCOE, *Consultant Psychiatrist, Maudsley Hospital, London*

Principles of Family Systems in Family Medicine. Edited by Sergio Henso and Nellie P. Grose. New York: Brunner/Mazel. 1985. Pp. 423. $40.00.

It is being said by Minuchin and others in the field of family therapy that there has been a failure of family therapy linked to its success. It has become well accepted and taught in universities and hospitals but the institutions remain the same. There is still remarkably little systems view in the general management of patients. This book sets about to remedy this by going against the trend of recent times of a "reductionist" approach to medical problems. The increased specialisation and emphasis on biological medicine has led doctors to be less interested in the person with the result that medical schools are turning out doctors who have difficulty in communication. This excellent book is addressed to GPs, mental health professionals, teachers and students of family medicine. The individual is clearly the unit of care and not the family because physicians treat individuals and the family is a rather arbitrary category, difficult to define. What is clear in any treatment of an illness is that the system of family and other networks surrounding that individual and his illness must be taken into account in any management of that illness. The book is divided into three, the first part dealing with the theoretical basis of systems theory, the second the common clinical issues in family medicine, and the third more specific clinical matters. The first section is fascinating and is recommended to anyone in the health field, including psychiatry. The only criticism of this section I would have is that the Minuchin chapter was taken from an article written some time ago and is more related to family therapy than family systems work. One important point to remember is that taking a broader systems view of problems does not involve more work but may, in fact, result in an eventual decrease in work.

The second part looks at the patient, the illness, the family and the physician as being part of a complex interaction and there is in it a very good chapter on the doctor/patient/family relationship. The other chapters include one on single adults, adolescents and care of the elderly, which are clearly areas likely to be found stressful by family practitioners.

The third part has a set of useful chapters on a variety of topics and conditions commonly found in general practice. These include drug abuse and death, and I did find the chapter on sexual difficulties particularly helpful.

This is a stimulating book, well edited, apart from occasional lapses, and it is an invaluable book to read and also to use as a reference. It is of particular interest to anybody involved at the interface of psychiatry and medicine. I was particularly pleased with the excellent referencing system and index. I only hope this book receives as wide an audience as it clearly deserves.

BRENCHLEY WILLIAM KNIGHTS, *Consultant Psychiatrist, Bethel Hospital, Norwich*

The History of Politics of Community Mental Health. By Murray Levine. New York: Oxford University Press. 1981. Pp. 232. £9.95.

Psychiatric Services for Underserved Rural Populations. Edited by L. Ralph Jones and Richard R. Parlour. New York: Brunner/Mazel. 1985. Pp. 303. $37.50.

The Family, the Patient and the Psychiatric Hospital. By The Committee for the Family (Group for the Advancement of Psychiatry). New York: Brunner/Mazel. 1985. Pp. 92. $11.95)pb). $17.50 (hb).

Levine's book on *Community Mental Health*, published in 1981, is reissued in paperback. Of course, community mental health is concerned with social and political issues rather than with the details of clinical care, which is the subject of community psychiatry. This scholarly and dispassionate study of mental health developments in the USA tells of President Kennedy's Mental Centers Act of 1963 and its outcomes. In doing so Levine analyses the nature of those historical, political, social and economic factors which lead to such change.

As our own Mental Health Commission begins to stretch itself, it is salutary to read the two chapters on the limitations of the law in relation to the implementation of change and community based services.

In his last chapter he considers President Carter's Commission on Mental Health which, among other things, drew attention to those who are unserved, underserved or inappropriately served. This includes not only racial minorities, the elderly and children but also inner city and rural populations.

Jones' and Parlour's book deals in nineteen short chapters with present day psychiatry in rural America. It is not all peace and fresh air, for violence is nearly as rife as in the city and disasters are commonplace. One whole chapter deals with the volcanic eruption of Mount St Helens. Social workers learn to open the jail while the sheriff drives another patient 400 miles to the nearest mental hospital. This is a land of disadvantaged ethnic minorities where even private telephone systems do not interconnect. The only hope of expanding the very limited services is through supporting and integrating the generalist health services and in mobilising the support of families in what are still often "rural" communities. But it is not rural psychiatry as we picture it; it is frontier psychiatry.

Families of patients everywhere might consider too that they are not being served very well (or not at all) by psychiatrists. Every candidate for the MRCPsych can cite the studies which George Brown began nearly 30 years ago on family influence on the patient with schizophrenia. But little or nothing has been changed to bring the family context into clinical practice.

The slim report from the Group for the Advancement of Psychiatry is a model of good writing, good sense and practical advice. It says nothing new but it may be important that the GAP has given its imprimature to a family approach on psychiatry.

Douglas Bennett, *Emeritus Physician, Bethlem Royal and Maudsley Hospital*

Psychopharmacology and Food. Edited by Merton Sandler and Trevor Silverstone. British Association for Psychopharmacology, Monograph No. 7. Oxford: Oxford University Press. 1985. Pp. 190. Price £20.00.

This book is like a small box of assorted chocolates. Its eleven essays, based on papers read at a 1983 symposium in London, range from reviews of the neurophysiology of feeding, of neuropeptides and food and water intake, of the psychopharmacology of centrally acting anorectic agents, through notes on diet and migraine, and psychotropic drugs, appetite and body weight, to an original clinical biochemical study of nutritional deficiencies in senile dements. Practically, the most valuable paper is on clinical use of anorectic drugs in obesity, followed by Russell's discussion of drugs for anorexia nervosa and bulimia. It is interesting to hear of the Hungarian work on Satietin, a glycoprotein which appears in plasma on feeding and seems to switch off eating activities.

Curzon gives a very clear account of the unexpected effects of starvation and of a high carbohydrate diet and insulin on brain 5HT in rats, which makes one wonder what happens in humans with diabetes mellitus or undergoing insulin sopor or coma treatment; and whether these changes in 5HT result in changed pharmacological responses.

This is the justification of a fragmentary collection, some items of which are rather indigestible. The best inform the clinician of scientific developments in relevant biological science, or stimulate the appetite for more by suggesting possible clinical application. But many aspects of the general subject are not covered: the influence of food on the absorption and liver metabolism of drugs, for instance, or the habit of zinc-deficient Turkish peasants of eating clay (are their responses to sulphonamides such as the anticonvulsant sulthiame thereby altered?). *Beta*, I think.

John Crammer, *Reader Emeritus in Biological Psychiatry, Institute of Psychiatry, London*

Neurophysiological Correlates of Mental Disorders. Edited by B. Saletu, C. Perris and D. Kemali. Basel: Karger. 1984. Pp. 111. $36.25.

This book is the fifteenth in a series on advances in biological psychiatry and is largely concerned with the analysis of electroencephalographic and evoked potential changes in psychiatric disorders. As such it represents the change that has taken place in psychophysiology over the past few years. Peripheral measurements are passé and the advances of high technology have allowed close examination of electrical changes in the brain.

Despite technological advance the average psychiatrist reading this volume would be hard put to find any chapter that might have a bearing on his clinical practice or provide a major boost to knowledge. Like Alice in *Through the Looking-Glass*, psychophysiology appears to be running as fast as it can to stay in the same place. Thus Bracale and his colleagues discuss evoked potentials in psychiatry, but their chapter betrays little significant progress since Dawson first described the averaging technique to obtain these potentials, Volavka describes the EEG in a criminal population and comes to the same conclusion as Denis Hill in 1942, and Schultes and his colleagues illustrate, like Duffy & Lacey in 1946, that patients who have bodily anxiety are centrally over-aroused.

However, there is one area in which psychophysiology may well provide some valuable insights: the study of inter-hemispheric asymmetry in the brain. The first three chapters by Flor-Henry, Gruzelier, Kemali and their co-workers are well worth reading, although it is difficult to integrate their conclusions. Flor-Henry has long maintained that there are important differences between the right and left hemispheres in manic-depressive psychosis and schizophrenia and he is now developing physiological evidence to support his clinical findings. He finds that energy oscillations between the right and left hemispheres are reduced in both schizophrenia and manic-depressive psychosis, with maximum reduction in schizophrenia. Gruzelier finds an excess of fast EEG activity in the left temporal region in schizophrenia and Kemali produces an interesting phylogenetic account of brain asymmetry in the shark, eel, newt, frog, lizard and mole.

I hope these findings will not be misinterpreted as evidence that the behaviour of schizophrenic patients represents regression to the primitive behaviour patterns possessed by these animals. I must confess to being tempted by these comparisons, as for years I have been trying to discover why one of my psychotic patients spends a large part of his day excavating his cellar in order to make tunnels underground.

Peter Tyrer, *Consultant Psychiatrist, Mapperley Hospital, Nottingham*

Modern Approaches to the Dementias. Part I: Etiology and Pathophysiology. Edited by F. Clifford Rose. Basel: S. Karger. 1985. Pp. 230. $67.25, SFr. 158.00, DM 189.00.

This is the first of two parts of the proceedings of an international symposium held in London in 1983, and it is the 19th of the series entitled Interdisciplinary Topics in Gerontology. The book is a welcome addition to this growing field. The organisers of the symposium and the editors are to be congratulated for bringing together international experts in the field, though sadly it has taken two years to publish.

In the main two types of papers are represented, some with the original research data and the other with reviews of the topic. The book is divided into four sections which deal with aetiology and genetics (five chapters), immunological factors (two chapters), pathology (five chapters) and neurotransmitter metabolism (seven chapters). A number of chapters concern topics of current interest in which there have been recent advances.

The review on genetic factors in Down's syndrome and their possible role in the pathogenesis of Alzheimer's disease is a succinct update with 79 references. Pick dementia: anatomical considerations and pathophysiological considerations is a scholarly review with excellent figures and clear, concise tables. Both chapters suggest possibilities for further research in the relevant fields. In contrast some articles are very basic, like the one on vascular disease and dementia. Overlap in a book of this kind with a multi-authored compilation of reviews, ideas and original research is to some extent inevitable. The book is sturdily bound and well printed, with a formidable number of references which occupy 52 of 230 pages. This volume is essentially for academics and researchers with an interest in the field of neurology, neuropathology and neurochemistry.

S. R. Kadambari, *Senior Registrar, St George's Hospital, London*

Modern Approaches to the Dementias. Part II: Clinical and Therapeutic Aspects. Edited by F. Clifford Rose. Basel: S. Karger. 1985. Pp. 227. £67.25, SFr158.00, DM189.00.

This is the second of two volumes recording the proceedings of an international symposium held at Charing Cross Hospital, London in the summer of 1983. It consists of 23 communications, some of them very short, on clinical aspects, diagnostic methods, epidemiology, treatment and patient care. Rather incongruously included among them are two papers from Trondheim (Norway) on the after-effects of stress in war sailors and in survivors of concentration camps: interesting but not relevant!

The chapters vary in substance, in quality and in novelty, as one has come to expect from conference proceedings. Some chapters are accounts of personal research, some are reviews and some are anecdotes of no general import. Fortunately, several of the papers have valuable things to say and the references form a most useful compendium of the recent literature on the many aspects of dementia discussed. The book deserves a place on the shelves of the less penurious medical libraries.

Loic Hemsi, *Consultant Psychiatrist, St George's Hospital, London*

Hormones and Human Behaviour. By Bernard T. Donovan. Cambridge: Cambridge University Press. 1985. Pp. 223. £25.00.

This book gives an authoritative account of the relationship between the endocrine and the nervous systems, and the manifestations of that relationship in behaviour. It will be of value to a wide range of clinicians and behavioural scientists in that it provides a review of work which would require a great deal of time and expertise to find and to assess. The emphasis is on neuroendocrine relationships rather than on details of their effects on behaviour, and this reflects the evidence which is available. The chapters on hormonal effects on emotion and on learning and memory, particularly, contain a lot of piecemeal material and lack the cohesiveness which might have been achieved if the discussion had been set, for example, in the framework of a theoretical model or models of behaviour.

Apart from a short section on depression, the work on psychiatric disorders is not brought together and has to be sought in various sections. In a technical area, of interest to many disciplines, a glossary would have been useful. Also, given the disjointed nature of the material and the often conflicting findings, brief, expert conclusions at the end of sections would have been invaluable. The only reference to the menopause is brief and this is surprising since this phase of clear-cut changes in hormonal levels, together with the widespread use of hormone therapy, is important for the study of the effects of hormones on a wide range of behaviours.

However, the book is informative; it presents an up-to-date account of existing work, and gives a glimpse of the developments which are emerging and which are bringing about radical changes in theoretical and applied approaches to the biological bases of behaviour.

DOREEN ASSO, *Principal Lecturer in Psychology, University of London Goldsmiths' College*

Ethical and Legal Issues in Counselling and Psychotherapy. Second edition. By WILLIAM H. VAN HOOSE and JEFFREY A. KOTTLER. London: Jossey-Bass. 1985. Pp. 258. £28.50.

I noted the title of this book and was full of anticipation. The ethical aspects of psychotherapy practice have deservedly won increasing attention in recent years and the literature is growing correspondingly. Yet the text for which we have all been waiting—one that covers the subject in both comprehensive and scholarly fashion—has not appeared. Would the book by Van Hoose and Kottler fill the need?

My suspicion arose when I read the subtitle—*A Comprehensive Guide*. Well, it might not be overly scholarly, but it might serve well as a practical sort of book for the clinician. I was a little sceptical however when I perused the book and discovered that of the 258 pages, only the first 170 consisted of text, while the rest was made up of an appendix containing various codes of ethics and an annotated bibliography. Finally, on reading these 170 pages, I confirmed my suspicions. A number of topics are addressed, but none receive detailed treatment. Moreover, the quality of the ethical arguments advanced is quite limited.

Consider the authors' concluding views on the therapist's use of deception (particularly as it is applied by some family therapists). Van Hoose and Kottler "believe" that "on the whole" it is "probably advantageous" [in what sense?] to resort to deception only when other therapeutic methods have been exhausted. They then stress that techniques of deception such as paradoxical instruction can be efficient and effective, but that they are "considerably less elegant" than methods which rely on the patient assuming responsibility for change. Less elegant? What has elegance to do with ethical justification?

The book's subtitle is even more of a misnomer when it comes to the legal issues. The ground covered is negligible with the focus chiefly on such topics as professional licensure and malpractice. Moreover, the account is virtually confined to the American context.

Thus, the question I posed at the outset as to whether this book fills the need of the psychotherapy profession for a sophisticated treatment of its ethical aspects must be answered in the negative. We shall have to continue to wait patiently.

SIDNEY BLOCH, *Consultant Psychotherapist and Clinical Lecturer in Psychiatry, University of Oxford and Warneford Hospital*

Endocoids: Proceedings of an International Symposium held in Fort Worth, Texas. May 23–26, 1984. Edited by HARBANS LAL, FRANK LABELLA and JOHN LANE. New York: Alan R. Liss. 1985. Pp. 541. £60.00.

An endocoid is an endogenous drug ("endo-akoid"). The brain contains receptors for drugs such as benzodiazepines and tricyclic antidepressants. Why? Does the brain also produce its own drugs? If so, are these better than the chemicals with which we treat our patients? Furthermore, might not a disturbance of these endogenous drugs underlie functional psychosis?

Such a line of thinking has led to the isolation of endogenous opiates and to a Nobel Prize for their discoverers. Now the hunt is on for the endogenous tranquilliser and the endogenous antidepressant. This book reviews these and other related searches. It is a long and frustrating business, and no-one knows when and if the endogenous psychotropes will be discovered. Last year it looked as if the endogenous antidepressant was going to be located exclusively within the pineal, as if our sanity hung on the end of the pineal stalk. Apparently this is not the case.

This book, which also reviews neuropeptides, is too technical to be appropriate for a small psychiatric library, but it is the most interesting book I have read this year.

STUART CHECKLEY, *Consultant Psychiatrist, Institute of Psychiatry, London*

AMERICAN JOURNAL OF PSYCHIATRY

Volume 143, Number 5 **May 1986**

Special Articles

561 The Dying Psychotherapist *Alex H. Kaplan and David Rothman*
573 The Treatment of Anorexia Nervosa *L. K. George Hsu*

Regular Articles

582 Comprehensive Analysis of Change After Brief Dynamic Psychotherapy *Mardi J. Horowitz, Charles R. Marmar, Daniel S. Weiss, Nancy B. Kaltreider, and Nancy R. Wilner*
590 Psychiatric Reactions to Disaster: The Mount St. Helens Experience *James H. Shore, Ellie L. Tatum, and William M, Vollmer*
596 ECT and Memory: Brief Pulse Versus Sine Wave *Larry R. Squire and Joyce A. Zouzounis*
602 Psychophysiological Evidence for Cerebral Laterality Effects in a High-Risk Sample of Students With Subsyndromal Bipolar Depressive Disorder *Rand E. Lenhart and Edward S. Katkin*
608 Posttraumatic Stress Disorder as an Insanity Defense: Medicolegal Quicksand *Landy F. Sparr and Roland M. Atkinson*
613 The Role of Proximity, Immediacy, and Expectancy in Frontline Treatment of Combat Stress Reaction Among Israelis in the Lebanon War *Zahava Solomon and Rami Benbenishty*
618 The Psychological Effects of Being a Prisoner of War: Forty Years After Release *Christopher C. Tennant, Kerry J. Goulston, and Owen F. Dent*

Commentary

622 Finding Psychiatric Diagnosis-Related Groups That Work: A Call for Research *Donald W. Light, Etienne J. Phipps, George E. Piper, David J. Rissmiller, Joseph N. Mobilio, and William F. Ranieri*

Editorial Brief Communications

625 The Journal "On-Line" *John C. Nemiah*
626 Is Briquet's Syndrome a Heterogeneous Disorder? *Barry Liskow, Ekkenhard Othmer, Elizabeth C. Penick, Cherilyn DeSouza, and William Gabrielli*
630 Childhood and Family Characteristics in Panic and Generalized Anxiety Disorders *Svenn Torgersen*
633 The Effect of Changing Thyroid Function on Cyclic Affective Illness in Human Subjects *Mark S. Bauer and Peter C. Whybrow*
637 An Annual Rhythm in the Battering of Women *Richard P. Michael and Doris Zumpe*

Clinical and Research Reports

641 Persistent Anticipatory Nausea, Vomiting, and Anxiety in Cured Hodgkin's Disease Patients After Completion of Chemotherapy *David F. Cella, Alison Pratt and Jimmie C. Holland*
643 Cocaine Precipitation of Panic Disorder *Thomas A. Aronson and Thomas J. Craig*
646 Lactate-Induced Panic in Primary Affective Disorder *Deborah S. Cowley, Stephen R. Dager, and David L. Dunner*
648 Focal Neurologic Symptoms in Panic Attacks *Patricia K. Coyle and Arnold B. Sterman*
650 Does Carbamazepine-Induced Reduction of Plasma Haloperidol Levels Worsen Psychotic Symptoms? *George W. Arana, Donald C. Goff, Hylar Friedman, Marjorie Ornsteen, David Greenblatt, Bruce Black, and Richard I. Shader*
652 Alprazolam-Induced Manic Episode in Two Patients With Panic Disorder *John C. Pecknold and Doris Fleury*
654 Insulin-Induced Hypoglycemia and Panic Attacks *Edward Schweizer, Andrew Winokur, and Karl Rickels*
656 Prevalence of the Rabbit Syndrome *Ramzy Yassa and Samarthji Lal*
658 Low Levels and Lack of Function of Muscarinic Binding Sites in Human Skin Fibroblasts From Five Affectively Ill Patients and Two Control Subjects *Siong-Chi Lin and Elliott Richelson*

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Index to Advertisers

Pharmaceuticals

The Boots Company plc	*facing* p 654
Brocades Limited	p ii
Geigy Pharmaceuticals	*facing* p 712
Janssen Pharmaceutical Limited	*facing* p 696
Labaz	*facing* p 701
Lundbeck Limited	*facing* pp 655 and 697
May & Baker Limited	*facing* p 700
E. R. Squibb Limited	*facing* pp 662 and 663
Upjohn Limited	*facing* p 696

Booksellers and Publishers

Harvard University Press	p ii
Hutchinson Publishers	p iii
International Clinical Psychopharmacology	*loose insert*
Raven Press	p iii
John Wiley & Sons Ltd	p vi

Clinics, Hospitals and Nursing Homes

St. Andrew's Hospital	p v
The Retreat	*inside back cover*

Appointments

Hospital for Sick Children	*facing* p 713
Illawarra Area Health Service	*facing* p 713
The World Health Organization	p iv
University of Auckland	p ii
University of Otago	p iv
University of Tasmania	p ii

Miscellaneous

Canadian Psychiatric Meeting	*facing* p 713
Charing Cross & Westminster Medical School	p iv

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THE BRITISH JOURNAL OF PSYCHIATRY

June 1986 Volume 148

Annotation

Dominance Hierarchies in Psychotherapy Groups; *James L. Kennedy and K. Royal Mackenzie* 625

Papers

Psychiatry in the People's Republic of China; *William Ll Parry-Jones* 632
Levels of Expressed Emotion and Relapse in Depressed Patients; *Jill M. Hooley, John Orley and John T. Teasdale* 642
Psycho-Social Predictors of Chronicity in Depressed Patients; *R. M. A. Hirschfeld, G. L. Klerman, N. C. Andreasen, P. J. Clayton and M. B. Keller* 648
Prevalence of the Fragile X Syndrome in an Institution for the Mentally Handicapped; *David A. Primrose, Rabia El-Matmati, Elizabeth Boyd, Christine Gosden and Marjorie Newton* 655
A Comparison of Drug-Related Problems in London Accident and Emergency Departments 1975–1982; *Hamid Ghodse, John Stapleton, Griffith Edwards, Thomas Bewley and Muhammad Al-Samarrai* 658
What happens when Psychiatric Out-Patients are seen Once Only? *Linda Gask* 663
Electroconvulsive Therapy as a Contributor to the Production of Delusional Misidentification; *George G. Hay* 667
The Nottingham Experiential Day in Psychotherapy: A New Approach to Teaching Psychotherapy to Medical Students; *Mark Aveline and Jane Price* 670
Electrocardiogram Changes and Therapeutic Desipramine and 2-Hydroxy-Desipramine Concentrations in Elderly Depressives; *S. P. Kutcher, K. Reid, J. D. Dubbin and K. I. Shulman* 676
Threatening Life Events in the Onset of Schizophrenia, Schizophreniform Psychosis and Hypomania; *R. K. Chung, P. Langeluddecke and C. Tennant* 680
The Epidemiology of Life Events and Long-Term Difficulties, with some Reflections on the Concept of Independence; *P. McC Miller, C. Dean, J. G. Ingham, N. B. Kreitman, S. P. Sashidharan and P. G. Surtees* 686
Alcoholism and the General Practitioner; *Alison Mowbray and Neil Kessel* 697
Does Propranolol have an Antipsychotic Effect? A Placebo Controlled Study in Acute Schizophrenia; *Rahul Manchanda and Steven R. Hirsch* 701
Ethnic Differences in Self-Poisoning: A Comparison of Asian and White Groups; *John Merrill and John Owens* 708

Comment

Causal Models in Psychiatric Research; *Matthew J. Edlund* 713

Brief Reports

Clovoxamine and Doxepin in Major Depressive Disorder: A Double-Blind Controlled Trial; *G. J. Lodge and Hugh L. Freeman* 718
Prolactin Response Induced by ECT and TRH; *Yiannis Papakostas, Manolis Markianos, George Papadimitriou and Costas Stefanis* 721
Comparison of the Prophylactic Action of Flupenthixol with Placebo in Lithium Treated Manic-Depressive Patients; *J. Esparon, J. Kolloori, G. J. Naylor, A. M. McHarg, A. H. W. Smith and S. E. Hopwood* 723
A Case of Parietal Lobe Atrophy; *Paul Dedman and Sharon Numa* 725
Unpredictability as a Correlate of Expressed Emotion in the Relatives of Schizophrenics; *Brigid MacCarthy, David Hemsley, Candy Schrank-Fernandez, Liz Kuipers and Randy Katz* 727
Asperger's Syndrome and Tourette Syndrome: The Case of the Pinball Wizard; *Jacob Kerbeshian and Larry Burd* 731
Lithium Augmentation in the Treatment of Delusional Depression; *M. Pai, A. C. White and A. G. Dean* 736
Locus of Control in Short and Long Sleepers; *Anand Kumar and A. K. Vaidya* 739

Correspondence 741

Book Reviews 754

Index to Volume 128 (January–June 1986) **to be published with the July issue**